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ENVIRONMENTAL QUALITY

ENVIRONMENTAL ASPECTS OF *ESCHERICHIA COLI* IN HUMAN HEALTH

by

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Prepared for the Subcommittee
on Biological Phenomena

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ENVIRONMENTAL ASPECTS OF ESCHERICHIA COLI IN HUMAN HEALTH

EXECUTIVE SUMMARY

This report provides detailed synopses of current knowledge of the following aspects of Escherichia coli: (1) genetic mechanisms, especially those concerned with plasmid-mediated transfer of antibiotic resistance and enterotoxin production due to a single plasmid; (2) human diseases arising from infections by E. coli or from the action of its enterotoxins; (3) quantitative data on E. coli in the Canadian environment and outbreaks of E. coli-induced human disease in Canada.

Of 11 plasmid-mediated properties of E. coli, enterotoxin production and antibiotic resistance are particularly important as hazards to human health. Enterotoxigenic E. coli of animal origin was first shown in Canada to be mediated by a single plasmid which also induced resistance to three antibiotics, and E. coli of human origin bearing plasmids with comparable attributes were subsequently described elsewhere. The importance of E. coli as a natural reservoir of plasmids is stressed. The plasmid-mediated transfer of certain biochemical attributes may create difficulties in the biochemical characterization of some E. coli isolates from human or environmental sources.

Human diseases attributable to E. coli are classified according to the major organ or system affected by the bacterium or its enterotoxins: (1) bacteremic disease affecting particularly newborns and elderly or immunocompromised patients; (2) urinary tract infections affecting a higher proportion of females than males in all age groups; (3) diarrheal disease (gastroenteritis) associated with (a) enteropathogenic serotypes, (b) heat-labile (LT) or heat-stable (ST) enterotoxin producers, and (c) enteroinvasive strains; and (4) diseases characterized by vascular injury due to a cytotoxin (VERO toxin) from E. coli.

QUANTITATIVE CANADIAN DATA ON ENVIRONMENTAL E. COLI AND ILLNESS

In Manitoba, 24% of 1217 patients who were hospitalized with acute infantile gastroenteritis from December 1973 to November 1975 excreted an enteric bacterial pathogen and 10% excreted an enteropathogenic E. coli, but only three isolates elaborated enterotoxins. Between November 1976 and January 1979, enterotoxigenic E. coli were recovered from 1.7% of the children and 1.5% of the adults with diarrhea, in contrast to 0.3% normal children and adults respectively.

In Nova Scotia during January and February 1978, E. coli O20a O20b:K84 spread rapidly throughout an infant medical ward in the absence of "enteric" isolation procedures. Fecal coliform counts reported in Nova Scotia in 1983, ranged from 1 to 4500 per 100 mL at an estuarine

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beach that was polluted by fecal wastes, while at a nearby non-polluted estuarine beach, maximum fecal coliform counts were 11 per 100 mL.

In Ontario, at freshwater beaches during summer 1962, no illness was reported among swimmers despite high mean coliform counts and low *E. coli* counts in lake water. Coliform counts in public swimming pools remained negligible with free residual chlorine at at least 0.6 $mg.L^{-1}$ or residual bromine concentrations of at least 2.0 to 4.0 $mg.L^{-1}$.

At Metropolitan Toronto beaches during 1979, median fecal coliform counts were 94 per 100 mL water and 170 per gm sediment when the waters were polluted by unchlorinated sewage effluent. Median counts in water and sediment were reduced to 17 and 110, respectively, after chlorination of effluent. Correlations were found between gastroenteritis among swimmers and fecal coliform counts at freshwater beaches both in Ontario and in the eastern United States, the latter showing a correlation coefficient of 0.804.

From 1978 through 1982, strains of *E. coli* 0157:H7 cytotoxic for VERO cells were isolated from cases of gastroenteritis in Ontario (4) and New Brunswick (2). Five patients developed hemorrhagic colitis. All isolates were negative for LT and ST enterotoxins and enteroinvasiveness. In 1982, in an outbreak of hemorrhagic colitis due to *E. coli* in Ottawa, Ontario, *E. coli* 0157:H7 was isolated from 18 of 31 patients and 2 of 117 staff at a nursing home. Prior to this, in August 1982, in Montreal, Quebec, a similar outbreak occurred among 4 patrons of a fast-food chain. *E. coli* 0157:H7 was suspected but was not isolated from the cases of hemorrhagic colitis or the food. In 1983, *E. coli* 0157:H7 was isolated from 2 of 17 patients with hemorrhagic colitis from the adjacent communities of Labrador City, Newfoundland and Labrador, and Fermont, Quebec. One positive case developed from each community. Between June and October of the same year, *E. coli* 0157:H7 was isolated from 18 patients with hemorrhagic colitis in Alberta. Three of these patients, children aged between 1 and 4 years, developed hemolytic uremic syndrome. In September 1983, *E. coli* 0157:H7 was isolated from a 4-year-old patient with hemolytic uremic syndrome in British Columbia.

Gaps in knowledge regarding Canadian data include: 1) lack of data on human disease incidence and *E. coli* in environmental freshwater used for domestic consumption by communities or privately; 2) lack of quantitative data regarding *E. coli* in environmental freshwater in provinces other than Ontario; 3) lack of published data on *E. coli* counts in regions where water is subject to persistent contamination by disposal of farm manure in agriculture; 4) absence of published data on the association between *E. coli* counts and chlorine or bromine concentrations in public swimming pools; 5) lack of data on proportions of *E. coli*-induced enterocolitis associated with LT and ST enterotoxin

producers; 6) failure to identify natural reservoirs of food-borne E. coli 0157:H7 associated with hemorrhagic colitis; and 7) absence of information on the correlation of E. coli R-factor incidence and E. coli-induced illness in Canadian communities.

Recommendations include: 1) the isolation, serotyping and assay of toxigenicity of E. coli in lakes and in streams used for domestic water supplies in the Atlantic, Central and Pacific regions of Canada; 2) the correlation of illness surveys among bathers at recreational and marine beaches with daily measurement of E. coli counts in water in provinces other than Ontario; 3) the establishment of a Canada-wide collaborative study to determine the incidence of enterotoxigenic strains among all serotypable E. coli isolates from patients with enterocolitis; 4) the determination of the prevalence and counts of various E. coli serotypes in drainage from feed lots and other animal-holding areas with particular attention to recreational waters that receive such drainage.

ENVIRONMENTAL ASPECTS OF *ESCHERICHIA COLI* IN HUMAN HEALTH

1.0 INTRODUCTION

Escherichia coli is a bacterium which affects our lives in a wide variety of ways: the organism is used as an indicator of fecal contamination; it is used as a convenient bacterium for the study of bacterial genetics and for the exploitation of developments in genetic engineering; and it is important as a cause of a wide range of diseases of man and animals.

The bacterium now known as *Escherichia coli* was recovered from feces by Theodore Escherich in 1885. The organism is a member of the family Enterobacteriaceae and as such shares with others the family characteristics. It is a gram-negative, rod-shaped bacterium, which is facultatively anaerobic. Biochemically, it is oxidase negative, and capable of reducing nitrates to nitrites. Further biochemical characteristics useful in identifying the species are listed in Table 1-1. *E. coli* strains show considerable variation in individual biochemical reactions and often a battery of tests is needed to obtain positive identification. *E. coli* is included under the term "coliform" which refers to the prompt lactose-fermenters in the family Enterobacteriaceae.

The considerable diversity of members of the species *E. coli* is recognized by a number of schemes which identify strains beyond the species level. The best developed of these is the serotyping scheme. In the international scheme, isolates are identified on the bases of their somatic or cell wall (O), their capsular (K) and their flagellar (H) antigens. At present, approximately 160 O, 100 K and 50 H antigens are recognized. An excellent review, including new interpretations of old concepts of *E. coli* serology, has been published by Ørskov *et al.* (1977). Many isolates of *E. coli* possess surface antigens that are not recognized in the international scheme, but there is understandable reluctance to add them to the system unless the isolates appear to have some special properties to justify the designation of new antigens. Fimbrial (fringe-like) structures, distinct from flagella, constitute important surface antigens on certain *E. coli* and have, in some cases, been included with the K antigens.

Other schemes for characterizing isolates of *E. coli* include phage typing, colicin typing, biotyping and resistogram typing (based on patterns of susceptibility to antimicrobial drugs).

Table 1-1. Selected biochemical properties of *Escherichia coli* (derived from Edwards and Ewing 1972).

Test	Reaction
Indole	+
Methyl Red	+
Voges-Proskauer	-
Citrate	-
Lactose	+
Gas from glucose	+
H_2S	-
Lysine decarboxylase	+
Urease	-
Phenylalanine deaminase	-

2.0 FECAL E. COLI AS AN INDICATOR OF FECAL CONTAMINATION

Escherichia coli, a facultative anaerobe, is a prominent member of the aerobic flora of the intestinal tract of man and animals, although it is outnumbered about 1000:1 by the strict anaerobes. Most strains of E. coli taken by mouth do not cause disease. In addition to its presence in large numbers (of the order of 10^8 bacteria per gram) in feces, E. coli is readily cultured in the laboratory on simple bacteriological media. Selective indicator and differential media, such as MacConkey agar, eosin methylene blue agar and endo agar have been formulated to aid with the cultivation and isolation of colonies of E. coli or other members of the coliform group. For purposes of laboratory determination of fecal contamination of water, the total coliform group of microorganisms is considered to include all aerobic and facultatively anaerobic, gram-negative, non-sporeforming, cytochrome oxidase negative, rod-shaped bacteria that ferment lactose with gas formation within 48 hours at 35°C. The fecal coliform group is that portion of the total coliform group capable of forming gas within 24 hours at 44.5°C (APHA 1971). Total coliforms are the primary water quality indicator for drinking water, whereas fecal coliforms are the primary water quality indicator for recreational or raw water quality (Health and Welfare Canada 1978).

E. coli and other fecal bacteria are readily adaptable for use as indicators of fecal contamination of water supplies. The interest in detection of fecal contamination lies in the potential of water supplies to act as a vehicle for agents of infectious disease, such as Salmonella typhi, Vibrio cholerae, Shigella species, Salmonella species, Giardia lamblia, and enterotoxigenic E. coli (Brown and McLean 1967; Craun 1977). These agents may not be readily detectable in water samples because of their relatively low numbers. A program of monitoring fecal contamination of water supplies is intended to prevent epidemics rather than to track down the sources of contamination after the onset of the epidemic.

Bacteriological examination of water may be desirable for several reasons, including:

i) determination of the extent of treatment facilities necessary to produce safe drinking water;

ii) establishment of the sanitary status of water for recreational purposes;

iii) measurement of the effects of discharge of sewage into lakes, coastal waters or rivers; and

iv) monitoring of water supplies for evidence of fecal contamination by mammalian or avian species.

It is common practice to conduct tests to determine (i) the total number of bacteria per mL of water and (ii) the numbers of fecal coliforms per 100 mL. The concentration of bacteria in the sample may be determined by the standard plate count technique in which dilutions of the water sample are spread over the surface of a suitable agar medium and the number of colonies counted after incubation at 35-37°C for 24 h. One test for the coliform organisms is conducted by determining the presence of growth of coliforms in culture tubes and dilution flasks inoculated with a geometric dilution series (0.01, 0.1 1.0, 10.0 and 100 mL) of samples, from which a statistical estimate, the most probable number (MPN) of coliforms per 100 mL of water is derived. In a simpler and more effective method that determines the concentration of coliforms, 100 ml of water are passed through a membrane filter and the filter is incubated under conditions that permit growth and ready detection of coliform colonies. The results from these determinations are compared with standards of acceptability established by the public health authorities.

In recent years there has been increasing evidence that simple enumeration of the total coliform group of bacteria is not a good indicator of hazardous microbial pollution in untreated water (Dukta 1973). It has been suggested that counts of fecal coliforms (Escherichia coli, based on reactions in the indole, methyl red, Voges-Proskauer and citrate tests) and of fecal streptococci are more reliable, particularly if both types of bacteria are counted (Dukta 1973; Feachem 1974, 1975). The ratio of fecal coliforms to fecal streptococci (FC:FS ratio) has been used as an indicator of fecal pollution, but there is debate on the validity of this method on the grounds that these two organisms do not die away at identical rates (Feachem 1975). Feachem's studies (ibid.) indicate that initially high FC:FS values that fall reflect human contamination, whereas initially low ratios that rise indicate contamination by a non-human fecal source, e.g. urban runoff, wildlife, birds, farm animals, or food processing plants (abattoirs).

Brown and Clark (1975) investigated the possibility of creating a microbiological index of human pollution of water which might be more useful than the fecal coliform index and tried to determine the effect of climate on indicators of human fecal contamination of water. They concluded that counts of total coliforms, fecal coliforms and fecal streptococci should be used concomitantly as indicators of fecal contamination of water. They demonstrated that the survival of these organisms in water depended on temperature, pH and metallic ion content of the water.

Health and Welfare Canada (1978) recommends the following as the maximum acceptable levels of total coliform organisms in drinking water in Canada:

i) no sample should contain more than 10 total coliform organisms per 100 mL;

ii) not more than 10 percent of the samples taken in a 30-day period should show the presence of coliform organisms;

iii) not more than two consecutive samples from the same site should show the presence of coliform organisms;

iv) none of the coliform organisms detected should be fecal coliforms.

For recreational water, Health and Welfare Canada recommends a limit of 200 fecal coliforms per 100 mL of water (Tobin and Ward 1984).

3.0 E. COLI AND GENETIC STUDIES

Modern bacterial genetics may be considered to have started when Griffith (1928) studied the *in vivo* transformation of nonpathogenic, noncapsulated *Streptococcus pneumoniae* into pathogenic capsulated organisms. Although transformation was not demonstrated in *E. coli* until 1972 (Cohen *et al.* 1972), this bacterium has long been the most intensively studied in the field of bacterial genetics. As early as 1907, mutations in lactose fermentation by *E. coli* had been the subject of careful scientific investigation (Massini 1907). A resurgence of genetic studies with *E. coli* occurred in the 1940's with the investigations by Gray and Tatum (1944) and by Lederberg *et al.* (1951) who researched the biochemical and genetic bases of certain *E. coli* mutants.

The studies of Lederberg and his associates (Lederberg and Tatum 1946a, b; Lederberg 1947, 1949; Lederberg *et al.* 1951) culminated in the recognition of the process of conjugation in *E. coli*. This finding opened the door to the extensive genetic analysis of the *E. coli* chromosome and to a more precise association of genetic change and biochemical effects. Recognition by Hayes (1953) of the nature and occurrence of the sex factor F in *E. coli* marked the beginning of the plasmid era, during which the marked genetic versatility of bacteria for survival as well as their potential for contributing to our welfare through genetic engineering has been demonstrated.

The phenomenon of multiple drug resistance has been thoroughly studied in *E. coli* (Falkow 1975; Mitsuhashi 1976). It has been demonstrated that:

i) many of the genes for drug resistance are carried on self-replicating genetic elements (R plasmids or R factors) which are circles of DNA separate from the bacterial chromosome;

ii) a single R plasmid may determine resistance to several drugs;

iii) one bacterium may carry several R plasmids;

iv) R plasmids may be rapidly transferred from one bacterium to another.

Transfer of R plasmids has been shown to occur in the intestines of humans and animals (Mitsuhashi 1977; Gyles *et al.* 1978) and there has been a rapid evolution of multiple drug resistance in *E. coli* as well as in other members of the Enterobacteriaceae. Oral administration of antibiotics has played a key role in these

developments. There is good evidence that the oral administration of antimicrobial drugs not only promotes the relative growth of resistant bacteria but also facilitates the transfer of R plasmids from one bacterium to another in the intestine. Studies on the physiology of bacterial conjugation show that transfer of plasmids is inhibited by the conditions of Eh, pH and fatty acid concentration found normally in the intestine, and that these conditions are changed, to favor conjugation, after oral antibiotic treatment. Furthermore, several researchers have demonstrated that the transfer of R factors in the intestine either is not detected or occurs at very low levels in the absence of orally-administered antimicrobial drugs.

Many orally-administered drugs are excreted in active form and in significant quantity in the feces. Certainly, R-factor transfer and the selection of resistant bacteria can be expected to occur outside the body. In this connection, transfer factors active at ambient temperature rather than at body temperature are likely to be highly significant.

In enterotoxigenic E. coli of animal origin, the existence of a single plasmid with genes for enterotoxin production as well as for resistance to tetracyclines, streptomycin, sulfonamide and mercury, was demonstrated in Canada by Gyles et al. (1977). Subsequently, similar plasmids which code for both enterotoxin production and drug resistance have been demonstrated in E. coli of human origin (Scotland et al. 1979; Echeverria and Murphy 1980; Silver et al. 1980; Stieglitz et al. 1980). The frequency of occurrence of such recombinant plasmids is not known, but it is clear that drug usage will select not only for resistance but also for virulence in the presence of such plasmids.

E. coli may be a very important reservoir of plasmids. The large numbers of this organism in the intestine and in feces enhance the opportunities for plasmids to transfer to a wide variety of other pathogenic and nonpathogenic bacterial species.

Plasmids have been shown to carry the genes for a large number of properties, in addition to drug resistance, in E. coli (Table 3-1) (Smith 1976; Maas 1981). Many of these plasmid-mediated characteristics are responsible for confusion in the identification of the bacterium, for rendering pathogenic E. coli resistant to antimicrobial therapy or for increasing the virulence of the bacterium. For example, the donation of a plasmid with genes for lactose fermentation by E. coli to a strain of Salmonella will render the Salmonella undetectable in many schemes for recovery of Salmonella from feces. Similarly, the acquisition of plasmids for H_2S or urease production by E. coli results in aberrant biochemical reactions. The problem of multiple drug resistance in clinical isolates of E. coli is a serious one, especially in nosocomial (hospital transmitted) infections involving E. coli. Virulence factors in E. coli for which plasmids are known to code

Table 3-1. Selected plasmid-mediated properties in *Escherichia coli*.

Fertility	- the ability to transfer DNA by conjugation
Resistance to	- antibacterial drugs
	- heavy metal ions
Production of	- colicins
	- enterotoxins
	- pili involved in colonization
	- hemolysin
	- H_2S
	- urease
Fermentation of	- lactose
	- raffinose

include the plasmids for the production of enterotoxins and the plasmids for producing colonization pili.

The recognition of translocatable drug-resistance-producing genetic elements has led to new opportunities to create mutants in E. coli (Kleckner et al. 1977). These elements have the ability to be inserted into replicons at a large number of sites. By using a suitable vehicle for carrying the translocatable drug-resistance element, and by subsequently selecting against maintenance of the vehicle in a recipient bacterium, one may obtain recipient cells in which the element has translocated into the chromosome or another replicon in the cell. The insertion of the element can cause mutations in the replicon.

The entire field of genetic engineering has drawn heavily on our familiarity with the genetics of E. coli and carries the promise of profound changes in our lives. It opens the possibilities of using deoxyribonucleic acid (DNA) to correct genetic defects, and to treat cancer, and of using bacteria as convenient factories for producing biologicals of value to mankind. E. coli strain K-12, which is normally not pathogenic for humans or animals, has been modified to reduce further the possibility of pathogenicity. It has also been used as a host cell in which recombinant DNA molecules have been introduced. By joining fragments of DNA to plasmids and by introducing the chimeric plasmid into E. coli and monitoring the expression of the DNA fragment in the E. coli culture, one can identify the function of the DNA fragment. Bacteriophages may be used instead of plasmids as molecular vehicles for the introduction of DNA fragments into bacteria. Replication of the recombinant molecule along with bacterial host cells is a simple way to obtain quantities of a desired gene product. DNA from eukaryotic cells has been shown to be functional when incorporated into a suitable vehicle and introduced into a bacterium. Techniques have been developed to obtain mammalian genes used in these studies.

4.0 E. COLI AS A HUMAN PATHOGEN

4.1 INTRODUCTION

Although most strains of E. coli are nonpathogenic, certain strains are capable of producing disease in humans. Three different kinds of disease are produced by E. coli in man: bacteremia, urinary tract infection, and enterocolitis. Each kind of disease will be dealt with separately because the types of E. coli and the mechanisms involved in pathogenesis are different for each. The immune system plays an important role in diseases due to E. coli, particularly in infants. This subject has been reviewed by Hanson (1976).

4.1.1 E. COLI IN BACTEREMIC DISEASE

During the past two decades there have been reports indicating that gram-negative rod bacteremia has increased in frequency and that E. coli is the most important bacterium involved (Watt and Okubadejo 1967; Young et al. 1977; Kreger et al. 1980). Such infections commonly manifest themselves in individuals with underlying chronic disease (e.g. diabetes, cirrhosis, urinary tract infection or in those with impaired immune mechanisms. E. coli bacteremia is a problem likely to affect premature babies and in a high percentage of cases will cause meningitis.

E. coli is the most common isolate recovered from the cerebrospinal fluid (CSF) and is responsible for about 50% of cases of meningitis in newborn infants (Bortolussi et al. 1978). E. coli bacteria that possess a particular K antigen (K1) are frequently implicated in meningitis; 84% of these E. coli strains possess this antigen (Robbins et al. 1974). The K1 antigen is also detected with high frequency in neonatal septicemia without meningitis, as well as in pyelonephritis in children (Kaijser 1973; McCracken and Sarff 1974). Paterson (1980) has suggested that a deficiency of IgG_2 immunoglobulin in the premature infant is an important factor in susceptibility to E. coli with the K1 capsular antigen. It is interesting that the E. coli K1 capsular polysaccharide is antigenically identical to that of group B Neisseria meningitidis (Kasper et al. 1973), another organism that causes meningitis in humans. Bortolussi et al. (1979) compared the virulence of K1 and non-K1 types of E. coli in newborn rats and concluded that the K1 capsular polysaccharide appeared to be an important determinant for virulence but was not a factor in the sensitivity of E. coli strains to the bactericidal activity of serum. The association of the K1 antigen with virulence of E. coli in meningitis has been the subject of an excellent review by Wilfert (1978).

Minshew et al. (1978a) noted a high occurrence of hemagglutination of human erythrocytes by virulent extraintestinal E.

coli isolates obtained from blood, urine, sputum and miscellaneous infections. Several factors have been postulated to be important in the virulence of septicemic strains of E. coli. Kochan et al. (1977) showed in experimental systems that avirulent E. coli are unable to grow in mammalian serum whereas virulent ones are able to multiply in it. They attribute this to the ability of virulent E. coli to obtain iron from their host through the effects of iron-binding enterochelin and lipopolysaccharides present in large amounts on the bacterial cell walls.

Although isolates of E. coli from man and animals with bacteremic disease commonly produce colicin V, and the presence of colicin V enhances the virulence of invasive E. coli in animals (Smith 1974; Smith and Huggins 1976; Smith 1978), Minshew et al. (1978a) could find no correlation between ability to synthesize colicin V and the virulence of E. coli from extraintestinal infection.

Much of the symptomatology of the bacteremic disease is consistent with the effects of endotoxin. These effects include pyrexia, intravascular coagulation, and shock.

4.1.2 E. COLI IN URINARY TRACT INFECTION

The quantitative culture of urine samples is usually conducted to determine whether any bacteria present in the sample are at low levels consistent with contamination or at higher levels known to be associated with infection (Kass 1957). A concentration of 10^5 or more organisms per mL in a urine sample is an indicator of infection. E. coli is the bacterium most commonly implicated as a cause of urinary tract infection.

E. coli is recognized as the most frequent cause of urinary tract infection in infants, schoolchildren, pregnant women and hospitalized patients. In females the prevalence of urinary tract infection is considerably higher than in males. The bacteria gain entrance to the urinary tract by direct spread from the large bowel and cause an ascending infection leading to their growth in the bladder. Further extension of the infection can lead to pyelonephritis.

There are two schools of thought concerning the characteristics of the E. coli strains that cause urinary tract infection. Several workers (Glynn et al. 1971; MacLaren 1975) have suggested that urinary tract pathogens constitute a subset of types of E. coli having special properties that endow them with virulence for the urinary tract. Others have suggested that the types of E. coli recovered from the urinary tract reflect those types that are most prevalent in the lower bowel (Kimball et al. 1964; Gruneberg et al. 1968; Brumfitt et al. 1971). Those who argue for specific pathogenicity relate urinary tract virulence to surface antigen (Dootson et al. 1973; Guze et al. 1973; Glynn and Nicholson 1975; Wong and Bettelheim 1976;

Kaijser et al. 1977), hemolysins (Fried et al. 1971; Cooke and Ewins 1975), adherence to epithelial cells (Eden et al. 1976; Hanson et al. 1977) or biochemical reactions (Guze et al. 1973; Kalmanson et al. 1975; Wong and Bettelheim 1976).

Although about 60% of E. coli from urinary tract infections have been shown to harbor plasmids, no association has been found between these plasmids and the virulence of the E. coli (Minshew et al. 1978b).

4.1.3 E. COLI AS A CAUSE OF DIARRHEAL DISEASE

Studies of the epidemiology of infantile diarrhea (gastroenteritis) due to E. coli were first reported from Europe. Lesage (1897) demonstrated that isolates of E. coli from infants involved in an outbreak of diarrhea could be agglutinated by serum from one infant with diarrhea whereas isolates of E. coli from unaffected individuals were not. Jensen (1897), who demonstrated the significance of the organism in "white scours" of young calves, is often credited as the first to study the role of E. coli in diarrhea. Some 30 years later, Adam (1923) used biochemical tests in attempts to identify which E. coli caused infantile diarrhea ("Dyspepsiekoli"). Others recognized the importance of identifying E. coli strains at a level beyond species in order that epidemiologic studies could be carried out. Goldschmidt (1933) was the first to apply systematic serological methods to this problem. Bray (1945) employed serological typing to identify the E. coli associated with a London outbreak of infantile diarrhea. Other workers, notably Giles and Sangster (1948) and Taylor et al. (1949), soon confirmed the usefulness of the serological approach to epidemiological studies of enterocolitis due to E. coli.

Although Kauffman's (1947) scheme for serological classification of E. coli placed the identification of E. coli serotypes on a sound footing, the need soon became evident to identify attributes of E. coli that correlated more closely than serological type with enteropathogenicity. Taylor et al. (1958) experimented with reactions of the bacteria in ligated segments of rabbit intestine and found that these reactions were a more precise indicator of enteropathogenicity than was serotype. Studies in animal systems, particularly by Smith and co-workers in England, led to three important observations: (i) diarrheagenic E. coli strains exhibit marked host specificity and studies in other than their natural host may be unrewarding; (ii) these strains colonize the small intestine; and (iii) they produce enterotoxins which cause diarrhea (Smith and Halls 1967a, b, 1968; Smith and Linggood 1971, 1972).

4.2 *E. COLI* ENTEROTOXINS

For many years *E. coli* was considered to cause diarrhea as a result of the endotoxin in the cell wall. The first successful attempt to demonstrate that a toxin distinctly different from endotoxin was the agent responsible for the diarrhea was reported by Smith and Halls (1967b) who demonstrated the existence of a heat-stable enterotoxin (ST) from porcine strains of enteropathogenic *E. coli*. Shortly thereafter, Gyles (1968) and Gyles and Barnum (1969) discovered a heat-labile enterotoxin (LT) in porcine enteropathogenic *E. coli* and showed that this toxin was related to cholera toxin. In 1970, Smith and Gyles (1970a) demonstrated that the ST and LT enterotoxins were different in several respects. Enterotoxins of the ST and LT types were subsequently demonstrated in human strains of diarrheagenic *E. coli* and of the ST type in bovine strains (Smith and Linggood 1972).

A considerable amount of research has been conducted on the LT enterotoxin. A summary of its major features is presented in Table 4-1. The similarities to cholera toxin are remarkable and exist even in the subunit structures of both toxins (Gyles 1974; Clements and Finkelstein 1978, 1979; Spicer *et al.* 1981).

Recent studies have identified subtle differences in amino acid sequences and antigenicity among LT from *E. coli* of human origin, LT from *E. coli* of porcine origin, and cholera toxin (Honda *et al.* 1981a, b; Geary *et al.* 1982).

E. coli LT acts in a manner apparently identical to the action of cholera toxin (Gill 1977). The toxin molecule has two major components, A and B. The A component contains the active site, whereas the B component contains the binding site and consists of five identical subunits. The toxin receptor has been identified as G_{M1} ganglioside. Toxicity requires holotoxin since there is a need for binding followed by activation. Broken cell test systems, however, require only the A component.

LT acts as an ADP(adenosine 5'-diphosphate)-ribosylating enzyme in much the same manner as cholera toxin, diphtheria toxin and *Pseudomonas aeruginosa* exotoxin. The toxin acts by catalyzing the transfer of ADP-ribose from NAD (nicotinamide adenine dinucleotide) to a GTP (guanosine 5'-triphosphate)-binding protein on the inner surface of the plasma membrane (Gill and Richardson 1980). The end product of this reaction is ADP-R-Protein-GTP, which binds the catalytic component of adenylate cyclase to form a complex (ADP-R-Protein-GTP-catalytic component). This complex synthesizes cyclic AMP (adenosine monophosphate) at an elevated rate as long as GTP remains bound.

The kinetics of LT action show that there is an initial lag of 15 minutes to 2 hours before intracellular cyclic AMP levels start to rise and that a peak level is attained within several hours, followed by

Table 4-1. Summary of properties of *Escherichia coli* heat-labile enterotoxin (LT)

Molecular weight	- 73 000
Chemical nature	- protein
Subunit structure	- A(30 000) (contains the active site); 4xB (11 000) (contains the binding site)
Heat stability	- activity reduced after 50°C for 30 minutes and almost completely destroyed after 90°C for 30 minutes
pH stability	- activity markedly impaired at pH 5 and lower and slightly reduced at pH 11
Time course of action	- delayed onset, prolonged
Mechanism of action	- stimulation of adenylate cyclase

a plateau which is maintained for the life of the cell. The elevated level of intracellular cyclic AMP in intestinal epithelial cells is responsible for net isotonic loss of fluid and electrolytes into the lumen of the gut. This is effected by active stimulation of secretion of Cl^-, Na^+, and HCO_3^- by crypt cells into the lumen as well as by inhibition of the influx of Na^+ and Cl^- into mature villus cells.

The genes which code for enterotoxin production in E. coli have been shown to be carried on plasmids (Smith and Halls 1968; Smith and Gyles 1970a; Skerman et al. 1972; Gyles et al. 1974). Among animal strains, plasmids appear to carry genes for ST only or for ST and LT (Smith and Gyles 1970a; Gyles 1971). Human strains of diarrheagenic E. coli plasmids code for genes for ST, LT or both. The genes for toxin production appear to be very stable among E. coli strains of animal origin but not among E. coli strains of human origin.

A variety of test systems may be used for the detection of LT. The system used in the earliest studies of ST is the ligated intestinal segment of rabbit or pig. The response in this test directly reflects the diarrheagenic effects of the toxin but the test is both low in sensitivity and inconvenient. Several tissue culture systems have been found to be satisfactory for detecting LT. These include YI adrenal cells (Donta et al. 1974), Chinese Hamster ovary (CHO) cells (Guerrant et al. 1974) and VERO cells (Speirs et al. 1977). Tests involving these systems are highly sensitive and convenient. Other tests include intradermal tests for increased vascular permeability (Evans et al. 1973b), tests with broken cell preparations (Gill et al. 1976), and tests involving Thiry-Vella loops in the jejunum of dogs (Sack et al. 1976), perfusion of rat intestine (Klipstein et al. 1978), and infections induced in infant rabbits by orogastric inoculation (Gorbach and Khurana 1971).

Two recent immunological procedures to detect enterotoxigenic E. coli are the Biken precipitin reaction test to detect LT (a modified Elek test) (Honda et al. 1981c) and the rapid latex particle agglutination test (LPAT) (Finkelstein and Yang 1983). Colony hybridization, based on gene probes produced from tox genes, has also been used for detection of enterotoxigenic E. coli (Moseley et al. 1982).

In tissue culture tests such as the YI adrenal cell test, two effects of the toxin may be observed. One is a steroidogenic effect on the cultured cells and the other is a morphologic change in those cells. The morphologic change is more readily observed and is most often used as the indicator of toxin activity. To facilitate this test it is possible to block the steroidogenic effect without inhibiting the morphogenic activity (Donta 1977).

So and co-workers (1974) reviewed the subject of extrachromosomal determinants of E. coli which contribute to bacterial pathogenicity. They noted that whereas 38 percent of E. coli not

associated with disease harbored at least one conjugative plasmid, the corresponding figure for enteropathogenic E. coli was 85 percent. So et al. (1975) demonstrated that E. coli enterotoxin plasmids that coded for both LT and ST had a majority of their polynucleotide sequences in common regardless of the origin of the strains from which the plasmids were isolated. They also found that these plasmids were related to plasmids of the FI and FII incompatibility groups.

Although in experimental studies the plasmids which code for production of enterotoxin can readily be transferred to a wide variety of serotypes of E. coli (Smith and Halls 1968; Smith and Gyles 1970a), there is in nature an association of the enterotoxin plasmids with certain serological groups of E. coli. This association has been documented in extensive epidemiologic and serologic studies conducted on animal isolates of enterotoxigenic E. coli (Gyles et al. 1971; Faikow et al. 1973; Gyles et al. 1974) and is now being shown for isolates of human origin (Evans et al. 1977; Merson et al. 1979).

Less research has been undertaken for the heat-stable enterotoxin but much is known about it. Table 4-2 summarizes the features of this type of toxin. Since 1978 evidence has been presented to show that there are at least two types of ST which have been identified as STa (or ST I) and STb (or ST II) (Burgess et al. 1978; Gyles 1979; Whipp et al. 1981).

In contrast to STb, STa is soluble in methanol, produces a positive test in the infant mouse assay and only a weak reaction in ileal loops in weaned pigs. Although bovine and human strains of enterotoxigenic E. coli produce STa only, porcine strains produce either one or both types of ST (Harnett and Gyles 1983). The mechanism of action of STb is not known, but STa is known to stimulate guanylate cyclase (Thomas and Knoop 1983; Field et al. 1978).

Three tests have been used for identification of ST: a ligated intestine test in pigs (Smith and Halls 1967a, 1967b; Smith and Gyles 1970a), a six-hour ligated intestine test in rabbits (Evans et al. 1973a) and the infant mouse test (Dean et al. 1972). All three depend on demonstration of fluid accumulation in the intestine. Researchers (Burgess et al. 1978; Gyles 1979) have differentiated between the response in the ligated pig intestine test in weaned pigs and that in a similar test in younger pigs.

The suckling mouse assay for ST has been well characterized by Giannella (1976) who found that the test was simple, rapid and highly reproducible. However, STb will not react in the infant mouse assay (Burgess et al. 1978; Gyles 1979). Ligated intestinal loops of mice have been described as susceptible to E. coli ST (Dobrescu and Huygelen 1973) but this test is not usually used. It appears to have no advantages and several disadvantages compared with the infant mouse test (Dean et al. 1972).

Table 4-2. Summary of properties of *Escherichia coli* heat-stable enterotoxin(s) (ST).

Molecular weight	- 2000 - 4000
Chemical nature	- protein
Absorption maximum	- 275 nm
Isoelectric point	- 3.9
Heat stability	- stable to 100°C for 10 min
pH stability	- stable between pH 2-11
Time course of action	- rapid onset, short duration
Mechanism of action	- stimulation of guanylate cyclase

In an outbreak of intestinal illness in the nursery of a hospital, the plasmid coding for the production of ST by an enterotoxigenic type of E. coli was identified by Wachsmuth et al. (1976). The molecular mass of the plasmid was 3 x 10^6 daltons and it was often cotransferred with another plasmid for drug resistance. The gene for ST I production has been cloned and amplified by So and co-workers (1976). The gene for ST II has also been cloned (Lee et al. 1983).

After purification of STa, its molecular mass ranged from 1972 daltons (Staples et al. 1980) to 3580 daltons (Alderete and Robertson 1978; Rao et al. 1981). Despite the heterogeneity in molecular size these molecules all contain a similar C-terminal 18-amino-acid sequence which includes six cysteine residues (So and McCarthy 1980; Chan and Giannella 1981).

STb has not been purified but genetic studies have been conducted to characterize the gene responsible for its production (Lee et al. 1983). Using gene cloning methods these workers have determined that STb is synthesized within the E. coli cell as a 71-amino-acid protein that contains a single peptide-like sequence. The sequence is quite different from that for STa.

Studies conducted by Levine et al. (1977) confirmed the significance of ST in diarrhea caused by E. coli strains that produce only ST. They fed doses of 10^6, 10^8 and 10^{10} ST^+ E. coli of human origin to volunteers. Three of five persons who received the dose of 10^8 ST^+ E. coli developed mild illness of a short duration (1 day), with abdominal pain and vomiting or diarrhea. Of the five individuals who received the 10^{10} dose, four developed serious diarrheal illness which lasted for 2 to 3 days.

4.3 COLONIZATION FACTORS

It is now recognized that in order to attain large numbers in the small intestine, E. coli needs to attach to the intestinal epithelium, thereby avoiding the cleansing action of peristalsis. This attachment is mediated by certain fimbriae. The first of these to be recognized were the K88 fimbriae on the surface of porcine enteropathogenic E. coli (Ørskov et al. 1961). Subsequently, the K99 fimbriae were detected on bovine enteropathogenic E. coli (Smith and Linggood 1972; Ørskov et al. 1975) and the colonization factor antigens CFA/I and CFA/II on human strains (Evans et al. 1975, 1979; Evans and Evans 1978). Colonization fimbriae called 987P have also been detected on certain porcine enteropathogenic E. coli (Nagy et al. 1977; Moon et al. 1980).

The K88 fimbriae have been studied more than the others. The genes for these fimbriae, as well as the K99 and CFA/I colonization fimbriae mentioned previously, are known to be carried on plasmids

(Ørskov et al. 1964; Evans et al. 1975; Smith 1976). It is likely that the other colonization fimbriae are also plasmid-mediated. Genes for raffinose fermentation are found on the K88 plasmids but their significance is not known (Smith and Parsell 1975; Shipley et al. 1978). The plasmid that codes for CFA on human diarrheagenic E. coli appears to code for ST as well. Three different antigenic configurations have been found for the K88 fimbriae: K88 a,b; K88 a,c; and K88 a,d (Guinee and Jansen 1979). These appear to represent the emergence of mutants under the pressure of selection by antibodies. The K88 fimbriae are produced on cultures grown at 37°C but not on cultures grown at 18°C. Attachment of K88-positive E. coli to intestinal epithelial cells may be prevented by specific antibodies (Jones and Rutter 1972; Rutter and Jones 1973; Wilson and Hohmann, 1974) and by competition for attachment sites (Davidson and Hirsch 1976).

The attachment fimbriae are also responsible for agglutination of certain red blood cells and hemagglutination may be used to detect them. Since Type 1 fimbriae, which are found very commonly on strains of E. coli, also cause hemagglutination, the mannose-sensitivity of Type 1 hemagglutination is used to differentiate this effect from that of the colonization fimbriae whose adherence to red blood cells is not blocked by D-mannose.

4.4 PATHOGENESIS

The essential features of pathogenesis appear to be the same for the various clinical forms of diarrhea due to nonenteroinvasive E. coli. A relatively large inoculum of a diarrheagenic E. coli appears to be necessary to initiate infection. High gastric pH, dietary factors, or malfunction of gastric acid secretion probably facilitate passage of large numbers of the bacteria into the small intestine. This area of the digestive tract is normally populated by low levels of bacteria but can be colonized by diarrheagenic E. coli. The presence of large numbers of diarrheagenic E. coli in the small intestine is thus one characteristic feature of the disease process (Koya et al. 1954; Thomson 1955). Although the attachment of the bacteria to the intestinal epithelial cells is an integral part of the colonization process, there must be other important factors related to growth and toxin production by the bacteria at this site. The production of toxic substances (enterotoxins) by the E. coli is responsible for the outpouring of fluid and electrolytes into the intestinal lumen.

4.5 ENTERIC DISEASE SYNDROMES

It is convenient to consider four diarrheal disease syndromes in humans caused by E. coli. These are epidemic infantile diarrhea, sporadic diarrhea, traveller's diarrhea and Shigella-like diarrhea. The

first three are caused by enterotoxigenic *E. coli* and the fourth by enteroinvasive *E. coli*.

The terminology that has developed is confusing. Many researchers reserve the term enteropathogenic for the *E. coli* implicated in epidemic infantile diarrhea, whereas the term enterotoxigenic is applied to other *E. coli* that cause diarrhea and can be shown to produce enterotoxin. The inference is that the epidemic infantile diarrhea types of *E. coli* do not produce enterotoxins. However, there is good evidence that epidemic infantile diarrhea types of *E. coli* do produce enterotoxins, although these enterotoxins may be different from those already characterized as LT and ST. In this discussion we will use the term diarrheagenic *E. coli* to refer to all the *E. coli* that cause diarrhea regardless of their mechanism for bringing about the diarrhea.

4.5.1 EPIDEMIC INFANTILE DIARRHEA

This syndrome refers to outbreaks of diarrhea occurring in epidemic fashion in infants under one year of age and caused by *E. coli* that belong to certain well-established serological types (EEC serotypes) (Table 4-3) and that are negative in the Chinese hamster ovarian cell (CHO), the YI mouse adrenal cell (YI) and the infant mouse tests for enterotoxigenicity (Kennedy *et al.* 1973; Gross *et al.* 1976a).

The pattern of disease is consistent with that expected of enterotoxigenic types of *E. coli* but these *E. coli* are noninvasive and give a negative Serény test. Furthermore, several workers have demonstrated some type of enterotoxigenicity in these *E. coli* (Smith and Gyles 1970a; Klipstein *et al.* 1978).

Smith and Gyles (1970b) injected sterile lysates of *E. coli* recovered from epidemic infantile diarrhea into ligated segments of rabbit intestine and demonstrated that a fluid response was often obtained. Furthermore, Smith and Linggood (1971) demonstrated that enterotoxin production in one of these *E. coli* (serogroup 026:K60) could be transferred to *E. coli* K-12 by mating donor and recipient cultures. A toxin with some of the properties of the enterotoxin of *Shigella dysenteriae* has been shown to be produced by certain *E. coli* of the classical infantile diarrhea types, as well as by certain *E. coli* which are pathogenic for the rabbit intestine but noninvasive and negative for ST and LT (O'Brien *et al.* 1977). Recently, Klipstein *et al.* (1978) demonstrated the presence of enterotoxins of the LT and ST types in the classical "enteropathogenic" types of *E. coli* recovered from well-documented outbreaks and tested by the rat perfusion method.

A plasmid-determined adhesive factor has been shown to occur on an *E. coli* implicated in epidemic infantile diarrhea (Williams *et al.* 1978).

Table 4-3. Serogroups of Escherichia coli considered to be classical enteropathogens[α] which cause epidemic infantile diarrhea.

026:K60	055:K59
086a:K61	0111:K58
0119:K69	0125:K70
0126:K71	0127a:K63
0142:H6	0124:K72

[α] A commercial supply of fluorescein-labelled E. coli antisera (Difco, Detroit, Michigan) includes antisera to all these serogroups except 0142:H6 and in addition provides for detection of E. coli of serogroups 018a 018b:K76; 018a 018b:K77; 020a 020b:K84; 020a 020c:K61; 028:K73; 044:K74; 0112a 0112b:K68; 0112a 0112b:K66; 0113:K75; 0128:K67; 0136:K78 and 0114:K90. Fluorescein-labelled polyantisera (1979-80 catalogue) for serogroups 026:K60; 055:K59, 0127a:K63 poly A; 086a:K61, 0119:K69, 0124:K72, 0125:K70, 0126:K71, 0128:K67 poly B; 018a 018c:K77, 020a 020c:K68, 020a 020b:K84, 044:K74, 0112a 0112c:K66 are also available.

Levine et al. (1978) demonstrated that E. coli strains implicated in epidemic infantile diarrhea could cause diarrhea when volunteers were fed E. coli inoculum in high doses (10^6 to 10^{10} organisms) although these strains were negative in conventional tests for LT, ST and invasiveness. Similar positive results in volunteer studies had been obtained by Kirby et al. (1950) and by Ferguson and June (1952).

The epidemic infantile diarrhea syndrome is well-established and the E. coli can be identified reliably by a combination of recognition of the syndrome and serological tests on the isolates (Rowe et al. 1974). These serological tests take the form of simple slide agglutination tests on isolated E. coli or fluorescent antibody tests on fecal smears. The widespread use of these procedures in North America has led to considerable frustration because positive results are obtained in only a small percentage of cases of diarrhea in children. This is due, in part, to the inappropriate use of these methods to identify the causal organism of diarrheal diseases which are quite different from epidemic infantile diarrhea (e.g. rotavirus, reovirus, etc.). It should be borne in mind that the prevalence of this disease syndrome is much higher in Europe than in Canada and the United States. To make matters worse, a significant percentage of E. coli isolates have been misidentified as belonging to one or another of the classical serogroups of enteropathogenic E. coli (Farmer et al. 1977).

Diarrhea in infants may also be caused by enterotoxin-producing types of E. coli different from those implicated in epidemic infantile diarrhea (Gross et al. 1976b; Guerrant et al. 1976; Ryder et al. 1976; Rowe et al. 1978) (Table 4-4).

The problems that arise from failure to differentiate the various syndromes have been pointed out by Goldschmidt and DuPont (1976). They tested 48 isolates of E. coli which had been recovered from children with diarrhea and which belonged to the O groups associated with infantile diarrhea. The conventional tests for LT, ST and invasiveness were conducted and most isolates gave negative results in all tests. These data do not constitute evidence of lack of correlation of serotype with pathogenicity; they indicate lack of correlation of serotype with results in these conventional tests.

4.5.2 SPORADIC DIARRHEA

Sporadic diarrhea (Gorbach and Khurana 1971) differs from epidemic infantile diarrhea in that (i) there is no evidence of an epidemic pattern, (ii) the E. coli implicated do not usually belong to the classical EEC serotypes and (iii) enterotoxin production is readily demonstrated by use of standard tests such as the tissue culture

Table 4-4. Serogroups of Escherichia coli of human origin frequently[α] associated with enterotoxicity.

O6:H16	O8:H9
O15:H11	O25:H42
O78:H11	O78:H12
O115:H40	O115:H51
O148	

α O groups less frequently encountered as human enterotoxigenic E. coli include groups 4, 7, 20, 27, 29, 34, 63, 85, 96, 114, 123, 126, 128 and 159.

(Chinese hamster ovary, YI adrenal or VERO cells) and the infant mouse test. The serotypes of E. coli associated with this syndrome are not well characterized at this time.

Farmer et al. (1977) dealt with the controversy over the merits of serological typing of E. coli recovered from sporadic cases of diarrhea in infants. They indicated that many of the isolates submitted by laboratories to the Center for Disease Control, Atlanta, Georgia, for confirmation as "enteropathogenic serotypes" did not belong to this category and that the laboratories were not following correct procedures for detecting these serotypes.

4.5.3 TRAVELLER'S DIARRHEA

Traveller's diarrhea (Gorbach et al. 1975) is similar to sporadic diarrhea but occurs among travellers to certain tropical and subtropical countries. The author includes in this syndrome cholera-like E. coli diarrhea (Finkelstein et al. 1976).

Traveller's diarrhea has been studied in American visitors to Kenya (Sack et al. 1977), Mexico (Gorbach and Khurana 1971; Merson et al. 1976; Morris et al. 1976; Donta et al. 1977) and Brazil (Shore et al. 1974) as well as in British soldiers in South Arabia (Rowe et al. 1970). In most cases the disease is of slight to moderate severity and causes inconvenience for one to five days. Occasionally, however, the severity is such as to produce a clinical picture identical to that seen in cholera (Finkelstein et al. 1976). Although this kind of disease is usually associated with travel, the same syndrome may be recognized in individuals who are indigenous to the area. A notable outbreak of epidemic diarrhea due to enterotoxigenic E. coli was reported to occur at a park in the United States (Rosenberg et al. 1977). This outbreak was associated with contaminated water supply and affected park staff as well as visitors.

Titers of antibody to the LT have been shown to rise to a significant degree in only those Peace Corps volunteers in Kenya who had diarrhea associated with excretion of LT-positive E. coli (Sack et al. 1977). In a similar study involving American students in Mexico, a rise in titer of antibody to LT was observed in more than 90 percent of the students who were excreting LT-producing E. coli (Lee and Kean 1978).

Low standards of hygiene are probably important for the occurrence of traveller's diarrhea, since travellers to warm climates with good sanitation do not usually develop diarrheal disease (Kean 1963; Ryder et al. 1977). It is also probable that prior exposure of travellers to diarrheal agents may offer some protection. Thus, travellers from countries with low levels of diarrheal disease are more

frequently affected than are travellers from countries with high levels (Haneveld 1960; Kean 1969; Loewenstein et al. 1973).

Contaminated food has been incriminated as an important source of infection (Tjoa et al. 1977). Although Nye (1979) has suggested that drinking water is an unlikely source of the organism because a high infective dose is necessary, there are precedents for water as a source of infection in E. coli diarrhea (Rosenberg et al. 1977).

Several studies have been conducted to evaluate antimicrobial prophylaxis for traveller's diarrhea (Nye 1979), and although no consensus has been reached, it appears that this approach is of limited value. Treatment of affected individuals with antimicrobials is not usually necessary since the disease characteristically runs a short, self-limiting course. In severe cases, rehydration with suitable fluids and electrolytes is indicated. The development of suitable electrolyte solutions for oral administration is one of the important consequences of research on the pathogenesis of E. coli enterotoxin-mediated diarrhea.

Although the syndromes described are convenient for our perception of the situation, there is sometimes an overlap. For example, the kinds of E. coli that usually produce sporadic diarrhea will occasionally be responsible for an epidemic of diarrhea in hospitalized infants (Guerrant et al. 1975, 1976; Ryder et al. 1976). Furthermore, E. coli strains that produce "traveller's diarrhea" in visitors may also produce "sporadic diarrhea" in the native population.

In view of the lack of recognition of a strong association between serotype and enterotoxigenicity in the E. coli from sporadic diarrhea and traveller's diarrhea, serological typing is of limited value in the detection of these E. coli. Detection is based on tests for enterotoxins.

4.5.4 SHIGELLA-LIKE [ENTEROINVASIVE] E. COLI DIARRHEA

E. coli strains that belong to a limited number of serologic groups (Table 4-5) are capable of producing dysentery in humans (Formal and Hornick 1978). These strains often exhibit properties that reflect a close relationship to Shigella. Such properties include a negative or slow lactose fermentation reaction, a lack of flagella, and an antigenic relationship to certain Shigella.

The E. coli in this group, like Shigella, are able to penetrate HeLa cells (DuPont et al. 1971), Hep-2 cells (Mehlman et al. 1977), and intestinal epithelial cells, and give a positive Serény test (Serény 1957). The multiplication of these bacteria in the mucosa of the colon can account for many of the signs and symptoms of the disease.

Table 4-5. O groups of *Escherichia coli* considered to be enteroinvasive.

028 ac	0112 ac
0124	0136
0143	0144
0152	0164

E. coli of O group 124 have been implicated in outbreaks of dysentery in Britain and continental Europe (Ewing and Gravatti 1947; Hobbs et al. 1949; Lanyi et al. 1959). In several of the outbreaks, contaminated water or food was identified as the source of infection. In 1971, the same O group was responsible for an outbreak of dysentery in the United States and was recovered from the food source, imported French cheese (Marier et al. 1973).

Fantasia et al. (1975) conducted studies on the detection and growth of enteropathogenic E. coli in soft-ripened cheese. They noted that certain invasive types of E. coli that may be found in cheese are non-lactose fermenters and may remain undetected in routine approaches to recover E. coli. They developed a cultural testing procedure designed to ensure recovery of lactose-negative as well as lactose-positive E. coli. Their studies emphasized the extent to which E. coli in cheese could multiply during storage. Depending on the initial counts and the temperature of storage, high levels of E. coli could be encountered in the absence of post-processing contamination. Samples of cheese with less than 10 organisms per gram had levels of 10^3 or 10^5 per gram after 10 days of storage at 4°C or room temperature respectively. When the initial counts were higher, the final counts were as high as 10^9 per gram even at 4°C.

4.6 DISEASES CHARACTERIZED BY VASCULAR INJURY

A number of diseases of man and animals associated with E. coli are characterized by damage to vascular endothelium. Much of the work in this field has been conducted by Canadian workers. Edema disease of swine has long been known to be caused by specific serogroups of E. coli (Sojka 1965) but experimental reproduction of the disease often included effects due to endotoxin in the crude toxic extracts of E. coli that were administered to the pigs. In Saskatoon, Saskatchewan, Clugston and associates (Clugston and Nielson 1974; Clugston et al. 1974) were able to separate a protein (edema disease principle) from strains of E. coli and to characterize the vascular injury which is responsible for the edema that typifies the disease.

There is evidence that a cytotoxin from E. coli may cause vascular damage, which is responsible for diarrhea and renal failure in hemolytic uremic syndrome in children, and for diarrhea in hemorrhagic colitis in humans (Karmali et al. 1983b). The cytotoxin appears to be identical or related to VERO toxin (VT) which was initially described by Konowalchuk et al. (1977).

O'Brien et al. (1977, 1982) used HeLa cells for studying cytotoxicity and demonstrated that high levels of cytotoxin were

produced by nonenterotoxigenic isolates of E. coli from infants with diarrhea. This Shiga-like toxin produced by E. coli was enterotoxic in rabbits, caused paralysis and death in mice and inhibited protein synthesis in HeLa cells.

It has recently been shown (Karmali et al. 1983a) that isolates of E. coli from edema disease of swine produce a cytotoxin. Studies are in progress to explore the relationships among these cytotoxins of E. coli as well as their relationship to the cytoxin from Shigella, reported by O'Brien et al. (1980).

5.0 EPIDEMIOLOGICAL DATA CONCERNING HUMAN ILLNESS ASSOCIATED WITH *E. COLI*, INCLUDING REFERENCES TO POSSIBLE ENVIRONMENTAL SOURCES OF *E. COLI*

5.1 MANITOBA

Among 1217 children who were hospitalized with a diagnosis of acute gastroenteritis at Children's Centre, Winnipeg between 1 December 1973 and 30 November 1975, including 1048 aged less than 36 months, 291 (24%) patients excreted an enteric bacterial pathogen, and 123 patients (10%) excreted an enteropathogenic *E. coli* (Gurwith and Williams 1977). No specific bacterial pathogen was found in 916 (76%) patients, but a rotavirus was visualized by electron microscopic examination in 45 of 342 (13%) of these patients in contrast to 9 of 130 (7%) patients who excreted a pathogenic bacterium. Only three isolates of *E. coli* elaborated either LT or ST enterotoxins. As with other bacterial pathogens, disease due to *E. coli* occurred more commonly during the warmer months of June through October. In contrast, rotavirus gastroenteritis occurred most commonly during the colder months of December through March.

In a group of 98 Winnipeg families comprising 166 children and 188 adults, together with 31 families comprising 80 children and 333 adults who lived at Berens River alongside Lake Winnipeg, 233 diarrheal and 1282 stool specimens were collected between November 1976 and January 1979 (Brunton *et al.* 1980). Another 374 diarrheal stools were collected from a group of 54 adults and 18 children. Results of tests examining 2227 subjects for enterotoxigenic strains of *E. coli* are given in Table 5-1. Isolates were assigned to 11 serotypes, of which 8 exhibited resistance to one or more antibiotics. *Aeromonas hydrophila*, which produced cytotoxic enterotoxin, was also isolated from 1 adult with cholera-like disease and from 6 children with mild diarrhea who also excreted enterotoxigenic *E. coli*. One strain of *Aeromonas hydrophila* was isolated from water collected from the Berens River.

5.2 NOVA SCOTIA

During January and February 1978, *E. coli* serotype O20a O20b:K84 was isolated from feces of 8 infants, 7 of whom had a diagnosis of gastroenteritis, in a medical ward in Halifax. The incubation period ranged from about 6 hours to 4 days and diarrhea persisted for 3 to 7 days (Richards *et al.* 1979). Gastroenteritis affected 6 infants with unrelated medical conditions following admission of the excreter of enteropathogenic *E. coli* on 16 January, and the last case occurred on 7 February. This exemplifies the rapidity and extent of nosocomial spread of *E. coli* in a general medical ward where "enteric" isolation

Table 5-1. Enterotoxigenic *Escherichia coli* in normal and diarrheal adults and children in Manitoba (from Brunton *et al.* 1980).

	Subjects excreting enterotoxigenic *Escherichia coli*	
	Number of total	Percent of total
Children		
Diarrheal	14/813	1.7
Normal	2/630	0.3
Adults		
Diarrheal	2/132	1.5
Normal	2/652	0.3
Total	20/2227	

procedures were not instituted. However enterotoxigenic E. coli was not transmitted from person to person among a group of adults who observed good hygienic practices in a closed community (Levine et al. 1980).

At an estuary that received fecal wastes, monthly counts (geometric means) of fecal coliforms ranged from 1 to 4500 per 100 mL at a sampling site within a recreational area (Robertson 1984). At monthly mean fecal coliform counts exceeding 2000 per 100 mL, Pseudomonas aeruginosa and Candida albicans were detected in 78% and 27% of the samples, respectively. However, when mean fecal coliform counts were below 200 per 100 mL, the frequency of detection of these other bacteria declined to 20% and 4.6%, respectively. At a nearby non-polluted estuary used for recreational bathing, maximum fecal coliform counts were 11 per 100 mL and other bacteria were detected in 2.3% of the samples.

5.3 ONTARIO

5.3.1 FRESHWATER BEACHES

At freshwater beaches along Lakes Ontario, Erie and Huron where bacteriological and clinical analyses were conducted on water samples collected during the summer of 1962, the total mean coliform counts ranged from 23 to 16 100 per 100 mL whereas mean counts of E. coli were 21-892 per 100 mL for Lake Ontario, 71-848 per 100 mL for Lake Erie and 0-1 per 100 mL for Lake Huron (Table 5-2). Visible debris such as seaweed and dead birds littered the beach near Hamilton, where the coliform count was 24 100 per 100 mL, yet the E. coli count was 382 and no appreciable illness was experienced by the numerous bathers questioned (Brown et al. 1963a). The pollution appeared to be mainly of non-human origin.

At a Lake Ontario recreational beach in Metropolitan Toronto during the summer of 1979 (Segfried et al. 1984) the overall median fecal coliform counts were 94 per 100 mL in the water and 170 per mL in the sediment. This beach was near the outflow pipe from a sewage treatment plant. Fecal coliform counts of 1.6×10^6 per 100 mL in raw sewage were reduced to 9.2×10^4 per 100 mL in unchlorinated effluent, and further reduced to 2.4×10^3 per 100 mL at the site of the outflow pipe. The water at the recreational beach contained 96 bacteria per 100 mL while the sediment showed 200 bacteria per 100 gm. When the effluent was chlorinated, the median fecal coliform content at the outflow pipe was 350 per 100 mL, water at the beach contained 17 per 100 mL and sediment showed 110 per 100 gm. Thus, dilution and dispersal of water were important factors in reducing the fecal coliform count; chlorination of effluent induced minimal additional reduction of the count. Cumulative results of bacteriological assays of water quality at Metropolitan Toronto beaches have shown that 63 to 95% of fecal

Table 5-2. Possible sources of coliforms in Ontario lakes.

Parameter	Lake Ontario (20 observations) Overall	Toronto	Hamilton	Lake Erie (8 obs.)	Lake Huron (7 obs.)	Small lakes (7 obs.)
Coliforms[α]	38-11 230	4400	24 100	232-16 000	23-13 500	93-11 500
E. coli[α]	21-892	1230	382	71-848	0-1	0-1060
Streptococcus fecalis[α]	2-20	31	3	38-49	1-5	20-67
Visible debris	+	+	++	+	-	±
Bathers	+	+	++	±	±	±
Cottages	++	++	+	++	-	++
Possible source	human	human	non-human	human	non-human	human

[α] Viable bacterial counts per 100 mL (MPN).

coliforms were identified as E. coli. Studies at recreational freshwater beaches in Ontario not contaminated by sewage effluent have suggested a statistically significant relationship ($p = 0.0058$) between fecal coliform concentrations and gastroenteritis among swimmers (Segfried and Brown 1983).

Significantly higher rates of gastroenteritis affected swimmers (compared with the background rates experienced by non-swimmers) who patronized seawater beaches near New York City during the summers of 1973 through 1975, when mean E. coli counts ranged from 30.5 to 278. However, insignificant differences were observed in gastroenteritis attack rates between swimmers and non-swimmers at lower mean E. coli counts (Cabelli et al. 1982).

A correlation coefficient for the association between gastroenteritis and E. coli counts was calculated to be 0.804 from data obtained from several freshwater beaches between 1979 and 1982 in Pennsylvania and Oklahoma (Dufour 1984). The regression equation showed that no swimmers were expected to contract gastroenteritis after bathing in water with E. coli counts of 18 per 100 mL, but that 0.7% were at risk of gastroenteritis when E. coli counts were 100 per mL.

5.3.2 SWIMMING POOLS

At public outdoor swimming pools in the City of Toronto during the summer of 1960, although standard filtration procedures eliminated coliforms on 15 of 17 occasions from water containing 2.2 to 39 coliforms per 100 mL, the coliform counts in pool water used by swimmers exceeded 15 when the free residual of chlorine was below 0.6 $mg.L^{-1}$ (McLean et al. 1961).

Between October and December 1962 at a small indoor swimming pool (capacity 200 000 L) in Toronto, coliform counts of 2.2 to 39 per 100 mL were observed in 5 of 10 water samples when the free and combined residual of bromine was 1.0 to 1.9 $mg.L^{-1}$; only 2 of 12 samples of water contained detectable coliforms with bromine residuals of 2.0 to 3.9 $mg.L^{-1}$, and none of 10 water samples yielded coliforms when bromine residuals were increased to between 4.0 and 9.0 $mg.L^{-1}$ (Brown et al. 1963b).

A large indoor swimming pool (capacity 540 000 L) in a Toronto suburb was disinfected with bromine between February and August 1963. The average number of bathers was 50 per hour during the daytime and 200 per hour during evenings. Coliform bacteria were detected in 21 of 115 water samples with bromine residuals below 2.0 $mg.L^{-1}$, but in only 4 of 27 samples when bromine residuals were between 2.0 and 6.0 $mg.L^{-1}$ (McLean et al. 1964).

5.3.3 FOOD

During November 1982, 31 of 353 residents of a home for the aged in Ottawa developed acute hemorrhagic colitis (Stewart et al. 1983). Symptoms included either watery diarrhea (74.1%) accompanied by blood (64.5%) and excessive mucus (45.2%) in the stools, or loose stools alone (25.8%), together with abdominal cramps (32.3%) and vomiting (9.7%). Symptoms of watery, blood-stained diarrhea persisted for 3 to 4 days in severe cases; loose stools were expelled by mild cases for 1 to 2 days. Most cases occurred between 11 and 16 November.

Escherichia coli 0157:H7 was isolated from 18 of 31 patients (58.1%), in most cases on the day of onset of diarrhea, and for as long as 11 days after onset. E. coli 0157:H7 was also isolated from 2 of 117 staff members; one experienced diarrhea for 6 days (November 17 to 22), but the other remained asymptomatic. Both staff members worked with patients on the wards. No food handlers excreted this bacterium. No other enteropathogenic bacteria or protozoa were isolated from either patients or staff.

A large quantity of hamburger had been purchased shortly before this outbreak, and portions had been served before and during the outbreak until 20 November. Attempts to isolate E. coli from samples of the hamburger gave negative results. During a similar outbreak in August 1982, E. coli 0157:H7 was isolated from stools of 4 patients in the United States who had contracted severe hemorrhagic colitis shortly after eating hamburgers (Uyeyama et al. 1982). Raw hamburger is commonly implicated in the transmission of human salmonellosis (Fontaine et al. 1978). Despite the failure to isolate E. coli from the hamburger in the Ottawa outbreak, the similarity of events to those of the United States outbreak led to the assumption, by some, that the hamburger was the most likely vehicle to suspect in the transmission of E. coli 0157:H7 isolated from patients and staff.

5.4 NEW BRUNSWICK AND ONTARIO

Between 1978 and October 1982, E. coli 0157:H7 was isolated from 4 cases of gastroenteritis in Ontario and 2 in New Brunswick; 5 cases had hemorrhagic colitis (Lior 1983). This serotype produced a cytotoxin for monkey kidney cells (VERO). All isolates from the Ottawa outbreak also produced VERO cytotoxin, but no isolates produced LT or ST enterotoxins, and no strain was enteroinvasive.

5.5 QUEBEC

In August 1982, prior to the Ottawa outbreak, 4 persons who consumed hamburger prepared at a restaurant of a fast-food chain in

Montreal developed acute hemorrhagic colitis. Although no enteric pathogen was recovered from any of the patients, the similarity of the outbreak to the United States outbreak again suggested that the infection may have been caused by E. coli 0157:H7. Once again, hamburger was suspected but not demonstrated to be the vehicle of transmission (Uyeyama et al. 1982; Lamothe et al. 1983).

5.6 NEWFOUNDLAND AND LABRADOR, AND QUEBEC

E. coli 0157:H7 was isolated from the feces of 2 of 16 patients with hemorrhagic colitis in May 1983. These patients were residents of Labrador City, Newfoundland and Labrador, and the nearby community of Fermont, Quebec (Hockin et al. 1983). No common exposure could be found in the Labrador City cases whereas most of the Fermont patients resided in one residential complex. Only one case from each community was positive for E. coli 0157:H7.

5.7 ALBERTA

Between June and October 1983, 18 patients from 15 families in southern Alberta contracted hemorrhagic colitis. E. coli 0157:H7 was isolated from the feces of each patient (Pai et al. 1983). All had watery diarrhea followed by hemorrhagic diarrhea with abdominal cramps, but no fever. Subsequently 3 children, aged 1 to 4 years, developed hemolytic uremic syndrome shortly after the onset of hemorrhagic colitis. Hamburgers purchased commercially and consumed by 8 of 14 patients within one day before the onset of diarrhea were not identified as a source of infection.

5.8 BRITISH COLUMBIA

A sporadic case of hemolytic uremic syndrome complicating hemorrhagic colitis affected a 4-year-old child in British Columbia during September 1983. A stool specimen yielded a strain of E. coli, identified as 0157:H7, and cytotoxic for VERO cells. No source of this strain was elicited from the history of the patient (Anderson et al. 1983).

6.0 GAPS IN KNOWLEDGE IN CANADIAN DATA AND RECOMMENDATIONS FOR RESEARCH

6.1 GAPS IN KNOWLEDGE

1) Lack of data regarding association between human disease and the presence of *E. coli* in environmental freshwater (lakes and streams) adjacent to and used by communities for domestic consumption.

2) Absence of longitudinal surveys of incidence of human gastrointestinal or other illness in bathers who use freshwater and marine beaches frequently during summer.

3) Lack of quantitative data concerning contamination of public or private drinking and recreational waters by disposal of farm manure in agriculture.

4) Absence of published data (e.g. with respect to the association between *E. coli* and halogen levels) from regions of Canada other than Ontario where regulations for minimum concentrations of free chlorine or bromine have been adopted for public swimming pools.

5) Lack of information on the proportion of patients with enterocolitis attributable solely to infection by strains of enterotoxic *E. coli*. To date, information is available for Manitoba only.

6) Failure to identify natural reservoirs of food-borne *E. coli* 0157:H7 associated with hemorrhagic colitis.

7) Absence of information concerning the incidence of R factors in environmental isolates of *E. coli* in Canadian localities where there is a significant rate of *E. coli* induced illness.

6.2 RECOMMENDATIONS FOR RESEARCH

1) Isolation, serotyping and assay of toxigenicity of *E. coli* in lakes and streams used for domestic water supplies in selected rural areas of provinces (apart from Manitoba where the resident human population is under continuing health surveillance), e.g. Lac La Ronge, Saskatchewan; Elliot Lake, Ontario.

2) Regular summertime illness surveys of bathers at (i) freshwater beaches, e.g. in the Ottawa region where *E. coli* counts are monitored routinely; (ii) marine beaches, e.g. in Vancouver where there are baseline data on microbial water quality. An Atlantic coastal area that can be surveyed microbiologically should also be included in the study.

3) Assay of enterotoxigenicity of all isolates of *E. coli* serotypes from patients with acute enterocolitis at selected regional hospitals throughout Canada.

4) Quantitative determination of *E. coli* serotypes in effluent from dairy barns, feed lots and chicken farms at the drainage entrance and at 20 m intervals from the drainage outflow point (MacLean 1983).

REFERENCES

Adam, A. 1923. Uber die Biologie der Dyspepsiekoli und ihre Beziehungen zur Pathogenese der Dyspepsie und Intoxikation. Jhrb. für. Kinderheilkund. 51: 295-315.

Alderete, J.F. and Robertson, D.C. 1978. Purification and chemical characterization of the heat-stable enterotoxin produced by porcine strains of enterotoxigenic Escherichia coli. Infect. Immun. 19(3): 1021-1030.

Anderson, J.D., Carter, J.E., Elmore, L. and MacLean, J.R. 1983. Hemolytic uremic syndrome and bloody diarrhea associated with a sorbitol-negative isolate of Escherichia coli 0157:H7 in a child-British Columbia. Can. Dis. Wkly Rep. 9: 173-174.

APHA. 1971. Standard methods for water and wastewater. 13th ed. American Public Health Association, Washington, D.C. 20036. pp. 636.

Bortolussi, R., Ferreiri, P. and Wannamaker, L.W. 1978. Dynamics of Escherichia coli infection and meningitis in infant rats. Infect. Immun. 22(2): 480-485.

Bortolussi, R., Ferrieri, P., Bjorksten, B. and Quie, R.G. 1979. Capsular K1 polysaccharide of Escherichia coli: Relationship to virulence in newborn rats and resistance to phagocytosis. Infect. Immun. 25(1): 293-298.

Bray, J. 1945. Isolation of antigenically homogeneous strains of Bact. coli Neapolitanum from summer diarrhoea of infants. J. Pathol. 57: 239-247.

Brown, J.R. and Clark, G.A. 1975. The effect of climate on indicators of human fecal contamination in water. National Health and Welfare Project #605-7-743-27(46).

Brown, J.R. and McLean, D.M. 1967. Waterborne diseases: An historical review. Med. Services J. Can. 23: 1011-1026.

Brown, J.R., McLean, D.M. and Nixon, M.C. 1963a. Swimming pools and bathing places in southern Ontario: Clinical and microbiological studies during 1962. Can. J. Public Health 54: 121-128.

Brown, J.R., McLean, D.M. and Nixon, M.C. 1963b. Bromine disinfection of swimming pools. Can. J. Public Health 54: 267-270.

Brumfitt, W., Faiers, M.C., Reeves, D.S. and Datta, N. 1971. Antibiotic resistant Escherichia coli causing urinary tract infection in general practice: Relation to faecal flora. Lancet 1(7694): 315-317.

Brunton, J., Hinde, D., Langston, C., Gross, R., Rowe, B. and Gurwith, M. 1980. Enterotoxigenic Escherichia coli in Central Canada. J. Clin. Microbiol. 11(4): 343-348.

Burgess, M.N., Bywater, R.J., Cowley, C.M., Mullan, N.A. and Newsome, P.M. 1978. Biological evaluation of a methanol-soluble, heat-stable Escherichia coli enterotoxin in infant mice, pigs, rabbits, and calves. Infect. Immun. 21(2): 526-531.

Cabelli, V.J., Dufour, A.P., McCabe, L.J. and Levin, M.A. 1982. Swimming-associated gastroenteritis and water quality. Am. J. Epidemiol. 115(4): 606-616.

Chan, S.K. and Giannella, R.A. 1981. Amino acid sequence of heat-stable enterotoxin produced by Escherichia coli pathogenic for man. J. Biol. Chem. 256(15): 7744-7746.

Clements, J.D. and Finkelstein, R.A. 1978. Immunological cross-reactivity between a heat-labile enterotoxin(s) of Escherichia coli and subunits of Vibrio cholerae enterotoxin. Infect. Immun. 21(3): 1036-1039.

Clements, J.D. and Finkelstein, R.A. 1979. Isolation and characterization of homogeneous heat-labile enterotoxins with high specific activity from Escherichia coli cultures. Infect. Immun. 24(3): 760-769.

Clugston, R.E. and Nielsen, N.O. 1974. Experimental edema disease of swine (E. coli enterotoxemia). I. Detection and preparation of an active principle. Can. J. Comp. Med. 38(1): 22-28.

Clugston, R.E., Nielsen, N.O. and Smith, D.L.T. 1974. Experimental edema disease of swine (E. coli enterotoxemia). III. Pathology and pathogenesis. Can. J. Comp. Med. 38(1): 34-43.

Cohen, S.N., Chang, A.C.Y. and Hsu, L. 1972. Nonchromosomal antibiotic resistance in bacteria: Genetic transformation of Escherichia coli by R-factor DNA. Proc. Natl. Acad. Sci. U.S.A. 69(8): 2110- 2114.

Cooke, E.M. and Ewins, S.P. 1975. Properties of strains of Escherichia coli isolated from a variety of sources. J. Med. Microbiol. 8(1): 107-111.

Craun, G.F. 1977. Waterborne outbreaks. J. Water Pollut. Control Fed. 1268-1279.

Davidson, J.N. and Hirsch, D.C. 1976. Bacterial competition as a means of preventing neonatal diarrhea in pigs. Infect. Immun. 13(6): 1773-1774.

Dean, A.G., Ching, Y., Williams, R.G. and Harden, L.B. 1972. Test for Escherichia coli enterotoxin using infant mice: Application in a study of diarrhea in children in Honolulu. J. Infect. Dis. 125(4): 407-411.

Dobrescu, L. and Huygelen, C. 1973. Susceptibility of the mouse intestine to heat-stable enterotoxin produced by enteropathogenic Escherichia coli of porcine origin. Appl. Microbiol. 26(3): 450-451.

Donta, S.T. 1977. Inhibition of the steroidogenic effects of cholera and Escherichia coli enterotoxins by iodoacetamide. Amer. Soc. Microbiol. Abstr. ann. meeting - 1977. B87. p. 30.

Donta, S.T., Moon, H.W. and Whipp, S.C. 1974. Detection of heat-labile Escherichia coli enterotoxin with the use of adrenal cells in tissue culture. Science. 183(4122): 334-336.

Donta, S.T., Wallace, R.B., Whipp, S.C. and Olarte, J. 1977. Enterotoxigenic Escherichia coli and diarrheal disease in Mexican children. J. Infect. Dis. 135(3): 482-485.

Dootson, P.H., MacLaren, D.M. and Titcombe, D.H.M. 1973. The distribution of urinary O-groups of Escherichia coli in urinary infections and in the normal faecal flora. In Urinary Tract Infection. Edited by W. Brumfitt and A.W. Asscher. Oxford University Press, London. pp. 139-145.

Dufour, A.P. 1984. Health effects criteria from fresh recreational waters. Cincinnati, Ohio. EPA-600/1-84.

Dukta, B.J. 1973. Coliforms are an inadequate index of water quality. J. Environ. Health. 36: 39-46.

DuPont, H.L., Formal, S.B., Hornick, R.B., Synder, M.J., Libonati, J.P., Sheahan, D.G., LaBrec, E.H. and Kalas, J.P. 1971. Pathogenesis of Escherichia coli diarrhoea. N. Engl. J. Med. 285(1): 1-9.

Echeverria, P. and Murphy, J.R. 1980. Enterotoxigenic Escherichia coli carrying plasmids coding for antibiotic resistance and enterotoxin production. J. Infect. Dis. 142(2): 273-278.

Eden, C.S., Hanson, L.A., Jodal, U., Lindberg, U. and Sohl Akerlund, A. 1976. Variable adherence to normal urinary tract epithelial cells of Escherichia coli strains associated with various forms of urinary tract infection. Lancet II(7984): 490-492.

Edwards, P.R. and Ewing, W.H. 1972. Identification of Enterobacteriaceae. Minneapolis: Burgess Publishing. 362 pp.

Evans, D.G. and Evans, D.J., Jr. 1978. New surface-associated heat-labile colonisation factor antigen (CFA/11) produced by enterotoxi- genic Escherichia coli of serogroups 06 and 08. Infect. Immun. 21(2): 638-647.

Evans, D.G., Evans, D.J., Jr. and Pierce, N.F. 1973a. Difference in the response of rabbit small intestine to heat-labile and heat-stable enterotoxins of Escherichia coli. Infect. Immun. 7(6): 873-880.

Evans, D.G., Silver, R.P., Evans, D.J., Jr., Chase, D.G. and Gorbach, S.L. 1975. Plasmid controlled colonization factor associated with virulence in Escherichia coli enterotoxigenic for humans. Infect. Immun. 12(13): 656-667.

Evans, D.J., Jr., Evans, D.G. and Gorbach, S.L. 1973b. Production of vascular permeability factor by enterotoxigenic Escherichia coli isolated from man. Infect. Immun. 8(5): 725-730.

Evans, D.J., Jr., Evans, D.G., DuPont, H.L., Ørskov, F. and Ørskov, I. 1977. Patterns of loss of enterotoxigenicity by Escherichia coli isolated from adults with diarrhoea: Suggestive evidence for an interrelationship with serotype. Infect. Immun. 17(1): 105-111.

Evans, D.J. Jr., Evans, D.G. and DuPont, H.L. 1979. Hemagglutination patterns of enterotoxigenic and enteropathogenic Escherichia coli determined with human, bovine, chicken, and guinea pig erythrocytes in the presence and absence of mannose. Infect. Immun. 23(2): 336-346.

Ewing, W.H. and Gravatti, J.L. 1947. Shigella types encountered in the Mediterranean area. J. Bacteriol. 53: 191-195.

Falkow, S. 1975. Infectious multiple drug resistance. Pion Ltd. London.

Falkow, S., Gyles, C., Skerman, F.J., So, M. and Guerry, P. 1973. The molecular nature of plasmids associated with enterotoxin production. Proc. Symp. on Cholera (1972). Tokyo, Japan. pp. 23-30.

Fantasia, L.D., Mestrandrea, L., Schrade, J.P. and Yager, J. 1975. Detection and growth of enteropathogenic Escherichia coli in soft ripened cheese. Appl. Microbiol. 29(2): 179-185.

Farmer, J.J., Davis, B.R., Cherry, W.B., Brenner, D.J., Dowell, V.R. Jr., and Balows, A. 1977. Enteropathogenic serotypes of Escherichia coli which really are not. J. Pediatr. 90(6): 1047-1049.

Feachem, R. 1974. Faecal coliforms and faecal streptococci in streams in the New Guinea Highlands. Water Res. 8(6): 367- 374.

Feachem, R. 1975. An improved role for faecal coliform to faecal streptococci ratios in the differentiation between human and non-human pollution sources. Water Res. 9(7): 689-690.

Ferguson, W.W. and June, R.C. 1952. Experiments on feeding adult volunteers with Escherichia coli 111. B., a coliform organism associated with infant diarrhoea. Am. J. Hyg. 55: 155-169.

Field, M., Graf, L.H., Laird, W.J. and Smith, P.L. 1978. Heat-stable enterotoxin of Escherichia coli: in vitro effects on guanylate cyclase activity, cyclic GMP concentration, and ion transport in small intestine. Proc. Natl. Acad. Sci. U.S.A. 75(6): 2800-2804.

Finkelstein, R.A. and Yang, Z.S. 1983. Rapid test for identification of heat-labile entertoxin-producing Escherichia coli colonies. J. Clin. Microbiol. 18(1): 23-28.

Finkelstein, R.A., Vasil, M.L., Jones, J.R., Anderson, R.A. and Barnard, T. 1976. Clinical cholera caused by enterotoxigenic Escherichia coli. J. Clin. Microbiol. 3(3): 382-384.

Fontaine, R.E., Arnon, S., Martin, W.T., Vernon, T.M. Jr., Gangarosa, E.J., Farmer, J.J. III, Moran, A.B., Silliker, J.H. and Decker, D.L. 1978. Raw hamburger: An interstate common source of human salmonellosis. Am. J. Epidemiol. 107(1): 36-45.

Formal, S.B. and Hornick, R.B. 1978. Invasive Escherichia coli. J. Infect. Dis. 137(5): 641-644.

Fried, F.A., Vermeulen, C.W., Ginsburg, M.J. and Cone, C.M. 1971. Etiology of pyelonephritis: further evidence associating the production of experimental pyelonephritis with hemolysis in Escherichia coli. J. Urol. 106(3): 351-354.

Geary, S.J., Marchlewicz, B.A. and Finkelstein, R.A. 1982. Comparison of heat-labile enterotoxins from porcine and human strains of Escherichia coli. Infect. Immun. 36(1): 215-220.

Giannella, R.A. 1976. Suckling mouse model for detection of heat-stable Escherichia coli enterotoxin: Characteristics of the model. Infect. Immun. 14(1): 95-99.

Giles, C. and Sangster, G. 1948. An outbreak of infantile gastro-enteritis in Aberdeen. The association of a special type of Bact. coli with the infection. J. Hyg. 46: 1-9.

Gill, D.M. 1977. Mechanism of action of cholera toxin. In Advances in cyclic nucleotide research. Edited by P. Greengard and G.A. Robison. Raven Press, New York. pp. 85-118, 574-575.

Gill, D.M. and Richardson, S.H. 1980. Adenosine diphosphate-ribosylation of adenylate cyclase catalyzed by the heat-labile enterotoxin of Escherichia coli: comparison with cholera toxin. J. Infect. Dis. 141(1): 64-70.

Gill, D.M., Evans, D.J. Jr. and Evans, D.G. 1976. Mechanism of activation of adenylate cyclase in vitro by polymyxin-released, heat-labile enterotoxin of Escherichia coli. J. Infect. Dis. 133(S): S103-S107.

Glynn, A.A. and Nicholson, A.M. 1975. Urinary-tract infection: localization and virulence of Escherichia coli. Lancet. 1(7901): 270-271.

Glynn, A.A., Brumfitt, W. and Howard, C.J. 1971. K-antigens of Escherichia coli and renal involvement in urinary tract infections. Lancet 1(7698): 514-516.

Goldschmidt, M.C. and DuPont, H.L. 1976. Enteropathogenic Escherichia coli: Lack of correlation of serotype with pathogenicity. J. Infect. Dis. 133(2): 153-156.

Goldschmidt, R. 1933. Untersuchurgen zur Atiologie der Durchfalser-krunkangen des Saughng. Jhrb. für Kinderheilkunde. 89: 318-358.

Gorbach, S.L. and Khurana, C.M. 1971. Toxigenic Escherichia coli - a cause of infantile diarrhoea in Chicago. N. Engl. J. Med. 287(16): 791-795.

Gorbach, S.L., Kean, B.H., Evans, D.G., Evans, D.J., Jr. and Bessudo, D. 1975. Travellers' diarrhoea and toxigenic Escherichia coli. N. Engl. J. Med. 292: 933-936.

Gray, C.H. and Tatum, E.L. 1944. X-ray induced growth factor requirements in bacteria. Nat. Acad. Sc. Proc. 30: 405-410.

Griffith, F. 1928. Significance of pneumococcal types. J. Hyg., Camb. 27: 574-575.

Gross, R.J., Scotland, S.M. and Rowe, B. 1976a. Enterotoxin testing of Escherichia coli causing epidemic infantile enteritis in the U.K. Lancet I(7960): 629-630.

Gross, R.J., Rowe, B., Henderson, A., Byatt, M.F. and MacLaurin, J.C. 1976b. A new Escherichia coli O group, O519, associated with outbreaks of enteritis in infants. Scand. J. Infect. Dis. 8(3): 195-198.

Gruneberg, R.N., Leigh, D.A. and Brumfitt, W. 1968. Escherichia coli serotypes in urinary tract infection: Studies in domiciliary, antenatal and hospital practice. In Urinary tract infection. Edited by F.O. Grady and W. Brumfitt. Oxford University Press, London. pp. 68-79.

Guerrant, R.L., Brunton, L.L., Schnaitman, T.C., Rebhun, L.I. and Gilman, A.G. 1974. Cyclic adenosine monophosphate and alteration of Chinese hamster ovary cell morphology: A rapid sensitive in vitro assay for the enterotoxins of Vibrio cholerae and Escherichia coli. Infect. Immun. 10(2): 320-327.

Guerrant, R.L., Moore, R.A., Kirschernfeld, P.M. and Sande, M.A. 1975. Role of toxigenic and invasive bacteria in acute diarrhea of childhood. N. Engl. J. Med. 293(12): 567-573.

Guerrant, R.L., Dickens, M.D., Wenzel, R.P. and Kapikian, A.Z. 1976. Toxigenic bacterial diarrhea: Nursery outbreak involving multiple bacterial strains. J. Pediatr. 89(6): 885-891.

Guinee, P.A.M. and Jansen, W.H. 1979. Behavior of Escherichia coli K antigens K88ab, K88ac, and K88ad in immunoelectrophoresis, double diffusion and hemagglutination. Infect. Immun. 23(3): 700-705.

Gurwith, M.J. and Williams, T.W. 1977. Gastroenteritis in children: A two-year review in Manitoba. I. Etiology. J. Infect. Dis. 136(2): 239-247.

Guze, L.B., Montgomerie, J.Z., Potter, C.S. and Kalmanson, G.M. 1973. Pyelonephritis: XVI. Correlates of parasite virulence in acute ascending Escherichia coli pyelonephritis in mice undergoing diuresis. Yale J. Biol. Med. 46(3): 203-211.

Gyles, C.L. 1968. Enterotoxicity of cell-free Escherichia coli preparations in ligated segments of pig's intestine. Ph.D. Thesis. Univ. of Guelph.

Gyles, C.L. 1971. Heat-labile and heat-stable forms of the enterotoxin from E. coli strains enteropathogenic for pigs. Ann. N.Y. Acad. Sci. 176: 314-322.

Gyles, C.L. 1974. Immunological study of the heat-labile enterotoxins of Escherichia coli and Vibrio cholerae. Infect. Immun. 9(3): 564-570.

Gyles, C.L. 1979. Limitations of the infant mouse test for Escherichia coli heat stable enterotoxin. Can. J. Comp. Med. 43(4): 371-379.

Gyles, C.L. and Barnum, D.A. 1969. A heat-labile enterotoxin from strains of Escherichia coli enteropathogenic for pigs. J. Infect. Dis. 120(4): 419-426.

Gyles, C.L., Stevens, J.B. and Craven, J.A. 1971. A study of Escherichia coli strains isolated from pigs with gastrointestinal disease. Can. J. Comp. Med. 35(3): 258-266.

Gyles, C.L., So, M. and Falkow, S. 1974. The enterotoxin plasmids of Escherichia coli. J. Infect. Dis. 130(1): 40-49.

Gyles, C.L., Palchaudhuri, S. and Maas, W.K. 1977. Naturally occurring plasmid carrying genes for enterotoxin production and drug resistance. Science 198(4313): 198-199.

Gyles, C.L., Falkow, S. and Rollins. L. 1978. In vivo transfer of an Escherichia coli enterotoxin plasmid possessing genes for drug resistance. Am. J. Vet. Res. 39(9): 1438-1441.

Haneveld, G.T. 1960. Some epidemiological aspects of travellers' diarrhoea in Lebanon. Trop. Geogr. Med. 12: 339-344.

Hanson, L.A. 1976. Escherichia coli infections in childhood - Significance of bacterial virulence and immune defence. Archiv. Dis. in Childhood. 51(10): 737-743.

Hanson, L.A., Ahlstedt, S., Fasth, A., Jodal, U., Kaijser, B., Larsson, P., Lindberg, U., Olling, S., Sohl-Akerlund, A. and Eden, C.S. 1977. Antigens of Escherichia coli. Human immune response, and the pathogenesis of urinary tract infections. J. Infect. Dis. 136(S): S144-S149.

Harnett, N.M. and Gyles, C.L. 1983. Enterotoxigenicity of bovine and porcine Escherichia coli of O groups 8, 9, 20, 64, 101 and X46. Am. J. Vet. Res. 44(7): 1210-1214.

Hayes, W. 1953. Observations on a transmissible agent determining sexual differentiation in Bact. coli. J. Gen. Microbiol. 8: 72-88.

Health and Welfare Canada. 1978. Guidelines for Canadian drinking water quality. 79 pp.

Hobbs, B.C., Thomas, E.M. and Taylor, J. 1949. School outbreak of gastroenteritis associated with a pathogenic paracolon bacillus. Lancet II: 530-532.

Hockin, J., March, S. and Ratman, S. 1983. Hemorrhagic colitis associated with Escherichia coli 0157:H7 - Newfoundland and Labrador. Can. Dis. Wkly. Rep. 9: 182-184.

Honda, T., Takeda, Y. and Miwatani, T. 1981a. Isolation of special antibodies which react only with homologous enterotoxins from Vibrio cholerae and enterotoxigenic Escherichia coli. Infect. Immun. 34(2): 333-336.

Honda, T., Tsuji, T., Takeda, Y. and Miwatani, T. 1981b. Immunological non-identity of heat-labile enterotoxins from human and porcine enterotoxigenic Escherichia coli. Infect. Immun. 34(2): 337-340.

Honda, T., Taga, S., Takeda, Y. and Miwatani, T. 1981c. Modified Elek test for detection of heat-labile enterotoxin of enterotoxigenic Escherichia coli. J. Clin. Microbiol. 13(1): 1-5.

Jensen, C.O. 1897. Cited by Sojka, W.J. In Escherichia coli in animals. Commonwealth Agricultural Bureaux. Farnham Royal, Bucks., England. 1965. p. 6.

Jones, G.W. and Rutter, J.M. 1972. Role of the K88 antigen in the pathogenesis on neonatal diarrhea caused by Escherichia coli in piglets. Infect. Immun. 6(6): 918-927.

Kaijser, B. 1973. Immunology of Escherichia coli: K antigen and its relation to urinary-tract infection. J. Infect. Dis. 127(6): 670-677.

Kaijser, B., Hanson, L.A., Jodal, U., Lidin-Janson, G. and Robbins, J.B. 1977. Frequency of E. coli K antigens in urinary-tract infections in children. Lancet I(8013): 663-666.

Kalmanson, G.M., Turck, M., Harwick, H.J. and Guze, L.B. 1975. Urinary-tract infection: Localization and virulence of Escherichia coli. Lancet I(7899): 134-136.

Karmali, M.A., Clarke, R. and Gyles, C.L. 1983a. Personal communication.

Karmali, M.A., Petric, M., Steele, B.T. and Lim, C. 1983b. Sporadic cases of hemolytic-uraemic syndrome associated with faecal cytotoxin and cytotoxin-producing Escherichia coli in stools. Lancet I(8325): 619-620.

Kasper, D.L., Winkelhake, J.L., Zollinger, W.D., Brandt, B.L. and Artenstein, M.S. 1973. Immunochemical similarity between polysaccharide antigens of Escherichia coli O7:-K1(L):NM and group B Neisseria meningitidis. J. Immunol. 110(1): 262-268.

Kass, E.H. 1957. Bacteriuria and the diagnosis of infections of the urinary tract. A.M.A. Arch. Intern. Med. 100: 709-714.

Kauffmann, F. 1947. The serology of the coli group J. Immunol. 57: 71-100.

Kean, B.H. 1963. The diarrhoea of travellers to Mexico. Summary of a five year study. Ann. Intern. Med. 59: 605-614.

Kean, B.H. 1969. Turista in Teheran. Traveller's Diarrhea at Eighth International Congresses of Tropical Medicine and Malaria. Lancet II(7620): 583-584.

Kennedy, D.H., Walker, G.H., Fallon, R.J., Boyd, J.F., Gross, R.J. and Rowe, B. 1973. An outbreak of infantile gastro-enteritis due to E. coli O142. J. Clin. Pathol. 26(10): 731-737.

Kimball, H., Turck, M. and Petersdorf, R.G. 1964. The epidemiology of nonenteric Escherichia coli infections. III. Relationship of E. coli antigens to experimental pyelonephritis. J. Lab. Clin. Med. 63: 907-913.

Kirby, A.C., Hall, E.G. and Coackley, W. 1950. Neonatal diarrhoea and vomiting outbreaks in the same maternity unit. Lancet II: 201-207.

Kleckner, N., Roth, J. and Botstein, D. 1977. Genetic engineering in vivo using translocatable drug-resistance elements: New methods in bacterial genetics. J. Mol. Biol. 116(1): 125-159.

Klipstein, F.A., Rowe, B., Engert, R.F., Short, H.B. and Gross, R.J. 1978. Enterotoxigenicity of enteropathogenic serotypes of Escherichia coli isolated from infants with epidemic diarrhea. Infect. Immun. 21(1): 171-178.

Kochan, I., Kvach, J.T. and Wiles, T.I. 1977. Virulence-associated acquisition of iron in mammalian serum by Escherichia coli. J. Infect. Dis. 135(4): 623-632.

Konowalchuk, J., Speirs, J.I. and Stavric, S. 1977. VERO response to a cytotoxin of Escherichia coli. Infect. Immun. 18(3): 775-779.

Koya, G., Kosakai, N., Kono, M. and Fukasawa, Y. 1954. Observations on the multiplication of Escherichia coli O111 B4 in the intestinal tract of adult volunteers in feeding experiments. The intubation study with Miller-Abbots double lumen tube. Jpn. J. Med. Sci. Biol. 7: 197-201.

Kreger, B.E., Craven, D.E., Carling, P.C. and McCabe, W.R. 1980. Gram-negative bacteremia. III. Reassessment of etiology, epidemiology and ecology in 612 patients. Am. J. Med. 68(3): 332-343.

Lamothe, F., Gaudreau, C., Bernard, D., Gill, S. 1983. Hemorrhagic colitis following the consumption of hamburgers - Quebec. Can. Dis. Wkly Rep. 9(13): 50-51.

Lanyi, B., Szita, J., Ringelham, B. and Kovãch, K. 1959. A water-borne outbreak of enteritis associated with Escherichia coli serotype 124:72:32. Acta Microbiol. Acad. Sci. Hung. 6: 77-83.

Lederberg, J. 1947. Gene recombination and linked segregation in Escherichia coli. Genetics 32: 505-525.

Lederberg, J. 1949. Aberrant heterozygotes in Escherichia coli. Proc. Natl. Acad. Sci. U.S.A. 35: 178-184.

Lederberg, J. and Tatum, E.L. 1946a. Novel genotypes in mixed cultures of biochemical mutants of bacteria. Cold Spring Harbor Symp. Quant. Biol. 11: 113-114.

Lederberg, J. and Tatum, E.L. 1946b. Gene recombination in E. coli. Nature (London) 158: 558.

Lederberg, J., Lederberg, E.M., Zinder, N.D. and Lively, E.R. 1951. Recombination analysis of bacterial heredity. Cold Spring Harbor Symp. Quant. Biol. 16: 413-443.

Lee, J.A. and Kean, B.H. 1978. International Conference on the diarrhea of travellers. New directions in research. J. Infect. Dis. 137(3): 355-369.

Lee, C.H., So, M., Moseley, S.L., Moon, H.W. and Gyles, C.L. 1983. Sequence analysis of E. coli enterotoxin STII gene. Abst. ann. meeting. Am. Soc. Microbiol. New Orleans, Louisiana.

Lesage, A.A. 1897. Contribution à l'étude des entérites infantiles; serodiagnostic; des races de Bacterium coli. Compte. Rend. des Séances de la Société de Biologie et ses Filiales. 49: 900-901.

Levine, M.M., Caplan, E.S., Waterman, D., Cash, R.A., Hornick, R.B. and Snyder, M.J. 1977. Diarrhea caused by Escherichia coli that produce only heat-stable enterotoxin. Infect. Immun. 17(1): 78- 82.

Levine, M.M., Nalin, D.R., Hornick, R.B., Bergquist, E.J., Waterman, D.H., Young, C.R., Sotman, S. and Rowe, B. 1978. Escherichia coli strains that cause diarrhoea but do not produce heat-labile or heat-stable enterotoxins and are non-evasive. Lancet I(8074): 1119-1122.

Levine, M.M., Rennels, M.B., Cisneros, L., Hughes, T.P., Nalin, D.R. and Young, C.R. 1980. Lack of person-to-person transmission of enterotoxigenic Escherichia coli despite close contact. Am. J. Epidemiol. 111(3): 347-355.

Lior, H. 1983. Comment on "Hemorrhagic colitis in a home for the aged - Ontario". Can. Dis. Wkly. Rep. 9(8): 32.

Loewenstein, M.S., Balows, A. and Gangarosa, E.J. 1973. Turista at an international congress in Mexico. Lancet I(7802): 529-531.

Maas, W.K. 1981. Genetic aspects of toxinogenesis in bacteria. Pharmacol. Therap. 13(1): 205-217.

MacLaren, D.M. 1975. Pyelonephritis and coliform infections of the urinary tract. Lancet 2(7934): 556.

MacLean, A.J. 1983. Pathogens of animals in manure: Environmental impact and public health. In Farm animal manures in the Canadian environment. Associate Committee on Scientific Criteria for Environmental Quality, NRCC No. 18976: 103-107.

Marier, R., Wells, J.G., Swanson, R.C., Callahan, W. and Mehlman, I.J.. 1973. An outbreak of enteropathogenic Escherichia coli foodborne disease traced to imported French cheese. Lancet II(7842): 1376-1378.

Massini, R. 1907. Uber einen in biologischer Beziehung interessanten Kolistamm (Bacterium coli mutabile). Ein Beitrag zur Variation bei Bacterien. Arch. Hyg. 61: 250-292.

McCracken, G.H. and Sarff, L.D. 1974. Current status and therapy of neonatal Escherichia coli meningitis. Hosp. Pract. 9(10): 57-64.

McLean, D.M., Brown, J.R. and Nixon, M.C. 1961. Microbiological and clinical investigations of outdoor public swimming pools. Can. J. Pub. Health 52: 61-67.

McLean, D.M., Brown, J.R. and Nixon, M.C. 1964. Microbiological hazards of freshwater bathing. Health Lab. Sc. 3: 151-158.

Mehlman, I.J., Eide, E.L., Sanders, A.C., Fishbein, M. and Aulisio, C.C.G. 1977. Methodology for recognition of invasive potential of Escherichia coli. J. Assoc. Off. Anal. Chem. 60(3): 546-562.

Merson, M.H., Morris, G.K., Sack, D.A., Wells, J.G., Feeley, J.C., Sack, R.B., Creech, W.B., Kapikian, A.Z. and Gangarosa, E.J. 1976. Travelers' diarrhea in Mexico. A prospective study of physicians and family members attending a congress. N. Engl. J. Med. 294(24): 1299-1305.

Merson, M.H., Ørskov, F., Ørskov, I., Sack, R.B., Huq, I. and Koster, F.T. 1979. Relationship between enterotoxin production and serotype in enterotoxigenic Escherichia coli. Infect. Immun. 23(2); 325-329.

Minshew, B.H., Jorgensen, J., Counts, G.W. and Falkow, S. 1978a. Association of hemolysin production, hemagglutination of human erythrocytes and virulence for chicken embryos of extraintestinal Escherichia coli isolates. Infect. Immun. 20(1): 50-54.

Minshew, B.H., Jorgensen, J., Swanstrum, M., Grootes-Reuvecamp, G.A. and Falkow, S. 1978b. Some characteristics of Escherichia coli strains isolated from extraintestinal infections of humans. J. Infect. Dis. 137(5): 648-654.

Mitsuhashi, S. 1976. (Editor.) Microbial Drug Resistance. Vol. 2. University Park Press, Baltimore. 439 pp.

Mitsuhashi, S. 1977. (Editor.) R Factor Drug Resistance Plasmid. University Park Press, Baltimore. pp. 4-5.

Moon, H.W., Kohler, E.M., Schneider, R.A. and Whipp, S.C. 1980. Prevalence of pilus antigens, enterotoxin types, and enteropathogenicity among K88-negative enterotoxigenic Escherichia coli from neonatal pigs. Infect. Immun. 27(1): 222-230.

Morris, G.K., Merson, M.H., Sack, D.A., Wells, J.G., Martin, W.T., DeWitt, W.E., Feeley, J.C., Sack, R.B. and Bessudo, D.M. 1976. Laboratory investigation of diarrhea in travelers to Mexico: Evaluation of methods for detecting enterotoxigenic Escherichia coli. J. Clin. Microbiol. 3(5): 486-495.

Moseley, S.L., Echeverria, P., Seriwatana, J., Tirapat, C., Chaicumpa, W., Sakoldaipeara, T. and Falkow, S. 1982. Identification of enterotoxigenic Escherichia coli by colony hybridization using three enterotoxin gene probes. J. Infect. Dis. 145(6): 863-869.

Nagy, B., Moon, H.W. and Isaacson, R.E. 1977. Colonization of porcine intestine by enterotoxigenic Escherichia coli: Selection of piliated forms in vivo, adhesion of pileated forms to epithelial cells in vitro, and incidence of a pilus antigen among porcine enteropathogenic Escherichia coli. Infect. Immun. 16(1): 344-352.

Nye, F.J. 1979. Travellers' diarrhoea. Clin. Gastroenterol. 8(3); 767-781.

O'Brien, A.D., Thompson, M.R., Cantley, J.R. and Formal, S.B. 1977. Production of a Shigella dysenteriae-like toxin by pathogenic Escherichia coli. Abst. ann. meeting. Am. Soc. Microbiol. Washington D.C.

O'Brien, A.D., LaVeck, G.D., Griffin, D.E. and Thompson, M.R. 1980. Characterization of Shigella dysenteriae 1 (Shiga) toxin purified by anti-Shiga toxin affinity chromatography. Infect. Immun. 30(1): 170-179.

O'Brien, A.D., LaVeck, G.D., Thompson, M.R. and Formal, S.B. 1982. Production of Shigella dysenteriae Type 1-like cytotoxin by Escherichia coli. J. Infect. Dis. 146(6): 763-769.

Ørskov, I., Ørskov, F., Sojka, W.J. and Leach, J.N. 1961. Simultaneous occurence of E. coli B and L antigens in strains from diseased swine. Influence of cultivation temperature on two new E. coli K antigens K87 and K88. Acta Pathol. Microbiol. Scand. 53: 404-422.

Ørskov, I., Ørskov, F., Sojka, W.J. and Wittig, W. 1964. K antigens K88ab(L) and K88ac(L) in E. coli. Acta Pathol. Microbiol. Scand. 62: 439-447.

Ørskov, I., Ørskov, F., Smith, H.W. and Sojka, W.J. 1975. The establishment of K99, a thermolabile transmissible Escherichia coli K antigen previously called "Kco", possessed by calf and lamb enteropathogenic strains. Acta Pathol. Microbiol. Scand., Sect. B 83(1): 31-36.

Ørskov, I., Ørskov, F., Jann, B. and Jann, K. 1977. Serology, chemistry, and genetics of O and K antigens of Escherichia coli. Bacteriol. Rev. 41(3): 667-710.

Pai, C.H., Gordon, R., Sims, H.V. and Bryan, L.E. 1983. Sporadic cases of hemorrhagic colitis associated with Escherichia coli 0157:H7 - Calgary, Alberta. Can. Dis. Wkly. Rep. 9: 181-182.

Paterson, P.Y. 1980. Central nervous system infection: general considerations. In The biologic and clinical basis of infectious diseases. Edited by G.P. Youmans, P.Y. Paterson, and H.M. Sommers. W.B. Saunders, Toronto. p. 585.

Rao, M.C., Orellana, S.A., Field, M., Robertson, D.C. and Gianella, R.A. 1981. Comparison of the biological actions of three purified heat-stable enterotoxins: Effects on ion transport and guanylate cyclase activity in rabbit ileum in vitro. Infect. Immun. 33(1): 165-170.

Richards, S.T., Wort, A.J. and Pointer, A.E. 1979. Nosocomial spread of enteropathogenic Escherichia coli - Nova Scotia. Can. Dis. Wkly. Rep. 5: 9-10.

Robbins, J.B., McCracken, G.H. Jr., Gotschlich, E.C., Ørskov, F., Ørskov, I. and Hanson, L.A. 1974. Escherichia coli K1 capsular polysaccharide associated with neonatal meningitis. N. Engl. J. Med. 290(22): 1216-1220.

Robertson, W.J. 1984. Pollution indicators and potential pathogenic microorganisms in estuarine recreational waters. Can. J. Pub. Health 75: 19-24.

Rosenberg, M.L., Koplan, J.P., Wachsmuth, I.K., Wells, J.G., Gangarosa, E.J., Guerrant, R.L. and Sack, D.A. 1977. Epidemic diarrhea at Crater Lake from enterotoxigenic Escherichia coli: A large water-borne outbreak. Ann. Intern. Med. 86(6): 714-718.

Rowe, B., Taylor, J. and Bettelheim, K.A. 1970. An investigation of travellers' diarrhoea. Lancet I(7636): 1-5.

Rowe, B., Gross, R.J., Lindop, R. and Baird, R.B. 1974. A new E. coli 'O' group 0158 associated with an outbreak of infantile enteritis. J. Clin. Pathol. 27: 832-833.

Rowe, B., Gross, R.J., Scotland, S.M., Wright, A.E., Shillom, G.N. and Hunter, N.J. 1978. Outbreak of infantile enteritis caused by enterotoxigenic Escherichia coli O6:H16. J. Clin. Pathol. 31(3): 217-219.

Rutter, J.M. and Jones, G.W. 1973. Protection against enteric disease caused by Escherichia coli - a model for vaccination with a virulence determinant. Nature 242(5399): 531-532.

Ryder, R.W., Wachsmuth, I.K., Buxton, A.E., Evans, D.G., DuPont, H.L., Mason, E. and Barrett, F.F. 1976. Infantile diarrhoea produced by heat-stable enterotoxigenic Escherichia coli. N. Eng. J. Med. 295(16): 849-853.

Ryder, R.W., Wells, J.G. and Gangarosa, E.J. 1977. A study of travellers' diarrhoea in foreign visitors to the United States. J. Infect. Dis. 136(4): 605-606.

Sack, D.A., Kaminsky, D.C., Sack, R.B., Wamola, I.A., Ørskov, F., Ørskov, I., Slack, R.C.B., Arthur, R.R. and Kapikian, A.Z. 1977. Enterotoxigenic Escherichia coli diarrhea of travelers: A prospective study of American Peace Corps volunteers. Johns Hopkins Med. J. 141(2): 63-70.

Sack, R.B., Johnson, J., Pierce, N.F., Keren, D.F. and Yardley, J.H. 1976. Challenge of dogs with live enterotoxigenic Escherichia coli and effects of repeated challenges on fluid secretion in jejunal Thiry-Vella loops. J. Infect. Dis. 134(1): 15-24.

Scotland, S.M., Gross, R.J., Cheasty, T. and Rowe, B. 1979. The occurrence of plasmids carrying genes for both enterotoxin production and drug resistance in Escherichia coli of human origin. J. Hyg. Camb. 83(3): 531-538.

Segfried, P.L. and Brown, N.E. 1983. The epidemiology of swimming-related illness at selected conservation areas. In Proceedings of the Technology Transfer Conference, Toronto, November 1983. p. 51.

Segfried, P.L., Brown, N.E., Cherwinsky, C.L., Jenkins, G.D., Cotter, D.A., Winner, J.M. and Tobin, R.S. 1984. Impact of sewage treatment plants on surface waters. Can. J. Public Health 75: 25-31.

Serény, B. 1957. Experimental keratoconjunctivitis shigellosa. Acta Microbiol. Acad. Sci. Hung. 4: 367-376.

Shipley, P.L., Gyles, C.L. and Falkow, S. 1978. Characterization of plasmids that encode for the K88 colonization antigen. Infect. Immun. 20(2): 559-566.

Shore, E.G., Dean, A.G., Holik, K.J. and Davis, B.R. 1974. Enterotoxin-producing Escherichia coli and diarrheal disease in adult travelers: A prospective study. J. Infect. Dis. 129(5): 577-582.

Silver, R.P., Aaronson, W. and Garow, C.F. 1980. Plasmids associated with an enterotoxigenic strain of E. coli. In Plasmids and transposons: Environmental effects and maintenance mechanisms. Edited by C. Stuttard and K.R. Rozee. Academic Press, New York. pp. 145-161.

Skerman, F.J., Formal, S.B. and Falkow, S. 1972. Plasmid-associated enterotoxin production in a strain of Escherichia coli isolated from humans. Infect. Immun. 5(4): 622-624.

Smith, H.W. 1974. A search for transmissible pathogenic characters in invasive strains of Escherichia coli: The discovery of a plasmid-controlled toxin and a plasmid-controlled lethal character closely associated, or identical, with colicine V. J. Gen. Microbiol. 83: 95-111.

Smith, H.W. 1976. Neonatal Escherichia coli infections in domestic animals: transmissibility of pathogenic characteristics. In Acute Diarrhoea in Childhood. Ciba Foundation Symposium 42. Elsevier. Amsterdam. pp. 45-72.

Smith, H.W. 1978. Transmissible pathogenic characteristics of invasive strains of Escherichia coli. J. Am. Vet. Med. Assoc. 173(5): 601-607.

Smith, H.W. and Gyles, C.L. 1970a. The relationship between two apparently different enterotoxins produced by enteropathogenic strains of Escherichia coli of porcine origin. J. Med. Microbiol. 3(3): 387-401.

Smith, H.W. and Gyles, C.L. 1970b. The effect of cell-free fluids prepared from cultures of human and animal enteropathogenic strains of Escherichia coli on ligated intestinal segments of rabbits and pigs. J. Med. Microbiol. 3(3): 403-409.

Smith, H.W. and Halls, S. 1967a. Observations by the ligated intestinal segment and oral inoculation methods on Escherichia coli infections in pigs, calves, lambs and rabbits. J. Pathol. Bacteriol. 93: 449-529.

Smith, H.W. and Halls, S. 1967b. Studies on Escherichia coli enterotoxin. J. Path. Bacteriol. 93: 531-543.

Smith, H.W. and Halls, S. 1968. The transmissible nature of the genetic factor in Escherichia coli that controls enterotoxin production. J. Gen. Microbiol. 52: 319-334.

Smith, H.W. and Huggins, M.B. 1976. Further observations on the association of the colicine V plasmid of Escherichia coli with pathogenicity and with survival in the alimentary tract. J. Gen. Microbiol. 92: 335-350.

Smith, H.W. and Linggood, M.A. 1971. Observations on the pathogenic properties of the K88, Hly and Ent plasmids of Escherichia coli with particular reference to porcine diarrhoea. J. Med. Microbiol. 4(4): 467-485.

Smith, H.W. and Linggood, M.A. 1972. Further observations on Escherichia coli enterotoxins with particular regard to those produced by atypical piglet strains and by calf and lamb strains: The transmissible nature of these enterotoxins and of a K antigen possessed by calf and lamb strains. J. Med. Microbiol. 5(2): 243-249.

Smith, H.W. and Parsell, Z. 1975. Transmissible substrate-utilizing ability in Enterobacteria. J. Gen. Microbiol. 87: 120-140.

So, M. and McCarthy, B.J. 1980. Nucleotide sequence of the bacterial transposon Tn 1681 encoding a heat-stable (ST) toxin and its identification in enterotoxigenic Escherichia coli strains. Proc. Natl. Acad. Sci. U.S.A. 77(7): 4011-4015.

So, M., Crandall, J.F., Crosa, J.H. and Falkow, S. 1974. Extrachromosomal determinants which contribute to bacterial pathogenicity. In Microbiology 1974. American Society for Microbiology. Washington, D.C. pp. 16-26.

So, M., Crosa, J.H. and Falkow, S. 1975. Polynucleotide sequence relationships among Ent plasmids and the relationship between Ent and other plasmids. J. Bacteriol. 121(1): 234-238.

So, M., Boyer, H.W., Betlach, M. and Falkow, S. 1976. Molecular cloning of an Escherichia coli plasmid determinant that encodes for the production of heat-stable enterotoxin. J. Bacteriol. 128(1): 463-472.

Sojka, W.J. 1965. Escherichia coli in animals. Commonwealth Agricultural Bureaux. Farnham Royal, Bucks., England.

Speirs, J.I., Stavric, S. and Konowalchuk, J. 1977. Assay of Escherichia coli heat-labile enterotoxin with VERO cells. Infect. Immun. 16(2): 517-622.

Spicer, E.K., Kavanaugh, W.M., Dallas, W.S., Falkow, S., Konisberg, W.H. and Schafer, D.E. 1981. Sequence homologies between A subunits of Escherichia coli and Vibrio cholerae enterotoxins. Proc. Natl. Acad. Sci. U.S.A. 78(1): 50-54.

Staples, S.J., Asher, S.E. and Gianella, R.A. 1980. Purification and characterization of heat-stable enterotoxin produced by a strain of Escherichia coli pathogenic for man. J. Biol. Chem. 255(10): 4716-4721.

Stewart, P.J., Desormeaux, W., Chene, J. 1983. Hemorrhagic colitis in a home for the aged - Ontario. Can. Dis. Wkly. Rep. 9(8): 29-32.

Stieglitz, H., Fonseca, R., Olarte, J. and Kupersztoch-Portnoy, Y.M. 1980. Linkage of heat-stable enterotoxin activity and ampicillin resistance in a plasmid isolated from an Escherichia coli strain of human origin. Infect. Immun. 30(2): 617-620.

Taylor, J., Powell, B.W. and Wright, J. 1949. Infantile diarrhoea and vomiting. A clinical and bacteriological investigation. Br. Med. J. 11: 117-125.

Taylor, J., Maltby, M.P. and Payne, J.M. 1958. Factors influencing the response of ligated rabbit gut segments to injected Escherichia coli. J. Pathol. Bacteriol. 76: 491-499.

Thomas, D.D. and Knoop, F.C. 1983. Effect of heat-stable enterotoxin of Escherichia coli on cultured mammalian cells. J. Infect. Dis. 147(3): 450-459.

Thomson, S. 1955. The role of certain varieties of Bacterium coli in gastro-enteritis of babies. J. Hyg. Camb. 53: 357-367.

Tjoa, W.S., DuPont, H.L., Sullivan, P., Pickering, L.K., Holguin, A.H., Olarte, J., Evans, D.G. and Evans, D.J. Jr. 1977. Location of food consumption and travelers' diarrhea. Am. J. Epidemiol. 106(1): 61-66.

Tobin, R.S. and Ward, W.M. 1984. Guidelines for Canadian recreational water quality. Can. J. Pub. Health 75: 15-18.

Uyeyama, R.R., Werner, S.B., Chin, S., Pearce, S.F., Kollip, C.L., Williams, L.P., Googins, J.A. 1982. Isolation of E. coli 0157:H7 from sporadic cases of hemorrhagic colitis - United States. Morb. Mort. Wkly. Rep. 31: 580-585.

Wachsmuth, I.K., Falkow, S. and Ryder, R.W. 1976. Plasmid-mediated properties of a heat-stable enteroxin-producing Escherichia coli associated with infantile diarrhea. Infect. Immun. 14(2): 403-407.

Watt, P.J. and Okubadejo, O.A. 1967. Changes in incidence and aetiology of bacteraemia arising in hospital practice. Br. Med. J. 1(5534): 210-211.

Whipp, S.C., Moon, H.W. and Argenzio, R.A. 1981. Comparison of enterotoxic activities of heat-stable enterotoxins from class 1 and class 2 Escherichia coli of swine origin. Infect. Immun. 31(1): 245- 251.

Wilfert, C.M. 1978. Escherichia coli meningitis: K1 antigen and virulence. Ann. Rev. Med. 29: 129-136.

Williams, P.H., Sedgwick, M.I., Evans, N., Turner, P.J., George, R.H. and McNeish, A.S. 1978. Adherence of an enteropathogenic strain of Escherichia coli to human intestinal mucosa is mediated by a colicinogenic conjugative plasmid. Infect. Immun. 22(2): 393-402.

Wilson, M.R. and Hohmann, A.W. 1974. Immunity to Escherichia coli in pigs: Adhesion of enteropathogenic Escherichia coli to isolated intestinal epithelial cells. Infect. Immun. 10(4): 776-782.

Wong, W.T. and Bettelheim, K.A. 1976. Serotypes of Escherichia coli from urinary tract infections in Hong Kong. Zentralbl. Bakteriol., Parasitenkd., Infektionskr. Hyg., Abt. 1. 236(4): 481-486.

Young, L.S., Martin, W.J., Meyor, R.D., Weinstein, R.J. and Anderson, E.T. 1977. Gram-negative rod bacteremia: microbiologic, immunological, and therapeutic considerations. Ann. Int. Med. 86(4): 456-471.

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